Cigna Medical Coverage Policy

Subject **Stem-Cell Transplantation for Adult Solid Tumors**

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Coverage Policy

Cigna covers single or tandem autologous hematopoietic stem-cell transplantation (HSCT) as medically necessary for relapsed or refractory testicular and ovarian germ cell tumors.

Cigna does not cover EITHER of the following procedures for the treatment of testicular cancer because they are considered experimental, investigational or unproven (this list may not be all inclusive):

- autologous HSCT as front-line therapy
- allogeneic HSCT

Cigna does not cover hematopoietic stem-cell transplantation for the treatment of ANY of the following solid tumors in an adult because it is considered experimental, investigational and unproven (this list may not be all-inclusive):

- soft tissue sarcoma
- cancer of the bile duct
- cancer of the cervix
- cancer of the colon and rectum

- cancer of the esophagus
- cancer of the gallbladder
- cancer of the lung
- cancer of the nasopharynx
- cancer of the pancreas
- cancer of the paranasal sinus
- cancer of the prostate
- cancer of the stomach (gastric cancer)
- cancer of the thymus
- cancer of the thyroid
- cancer of the uterus
- epithelial ovarian cancer
- melanoma
- renal cell carcinoma

General Background

Solid tumors in adults are a heterogeneous group of disorders encompassing a wide spectrum of body systems. Also called solid neoplasms, some tumors are chemoradiosensitive; however, many are not curable by chemotherapy and responses are often incomplete or not durable. Hematopoietic stem-cell transplantation (HSCT) has been proposed for the treatment of selected solid tumors in adults.

Stem-Cell Transplantation
Stem-cell transplantation refers to transplantation of hematopoietic stem cells (HSCs) from a donor into a recipient. HSC transplantation can be either autologous (i.e., using the patient's own stem cells) or allogeneic (i.e., using stem cells from a donor).

Dose intensification and autologous hematopoietic stem-cell transplantation (HSCT) is a strategy that has been proposed as a means to overcome inadequate response to standard dose chemotherapy. Although dose intensification has provided a survival advantage for selected individuals with hematologic malignancies, reviews of the efficacy of high-dose therapy in adult solid tumors have concluded that no role for this approach has been established, even in the diseases most sensitive to chemotherapy and radiation (Murren, 2005; Niebor, 2005).

Theoretically, allogeneic HSCT for solid tumors can induce a graft-versus-tumor (GVT) reaction in which the infused donor cells mount an immune response that eradicates the recipient's cancer cells. Early studies of ablative regimens for treatment of chemotherapy-refractory metastatic solid tumors demonstrated that the high doses of chemotherapy required to ablate the recipient's bone marrow lead to unacceptably high treatment-related mortality (TRM) rates of 20–35% (Arya, 2004).The high TRM associated with standard myeloablative regimens led to the study of non-myeloablative preparative regimens as conditioning for allogeneic stem-cell transplantation. These studies have not shown improved survival outcomes for participating patients and are limited by a lack of randomization, small patient populations, and limited follow-up. At this time, insufficient data are available to determine whether GVT effects can occur in most solid tumors (Storb, 2003).

Hematopoietic stem-cell transplantation (HSCT) for breast cancer is discussed in separate Coverage Policies (see Related Coverage Policy section). HSCT for the treatment of adult solid tumors including adult soft tissue sarcomas, cancers of the bile duct, cervix, colon, rectum, esophagus, gallbladder, lung, nasopharynx, pancreas, paranasal sinus, prostate, stomach (gastric cancer), thymus, thyroid, and uterus, epithelial ovarian cancer, malignant melanoma, renal cell carcinoma, and testicular and ovarian germ cell tumors are briefly discussed in this Coverage Policy.

Contraindications
Many factors affect the outcome of a tissue transplant; the selection process is designed to obtain the best result for each individual. The presence of any significant comorbid conditions which would significantly compromise clinical care and chances of survival is a contraindication to transplant. Relative contraindications to HSCT include, but are not limited to:

- poor cardiac function (ejection fraction < 45%)
- poor liver function (bilirubin > 2.0 mg/dl and transaminases greater than two times normal)
- poor renal function (creatinine clearance < 50 ml/min)
- poor pulmonary function (diffusion capacity [DLCO] < 60% of predicted)
- **EITHER** of the following:

  - presence of human immunodeficiency virus
  - an active form of **ANY ONE** of the following:

    - hepatitis B
    - hepatitis C
    - HTLV-1

- Karnofsky rating <60% and/or Eastern Cooperative Oncology Group (ECOG) performance status>2

Adult Soft Tissue Sarcoma: Soft tissue sarcomas may arise from the mesodermal tissues of the extremities, trunk and retroperitoneum, the head and neck, and rarely in the gastrointestinal stroma (National Cancer Institute [NCI], 2014a). Chemotherapy may be beneficial for patients with advanced sarcoma. Because treatment for this disease is evolving, participation in clinical trials is encouraged.

Literature Review
The effectiveness of hematopoietic stem-cell transplantation (HSCT) has not been demonstrated in high-quality randomized clinical trials (RCT). In one phase III RCT, Bui-Nguyen et al. (2012) reported results of 87 patients randomized to receive two doses of standard-dose chemotherapy or two doses of high-dose chemotherapy. The authors report that futility analyses led to study closure. Three-year overall survival (OS) was 49.4% for the standard-dose group versus 32.7% for the patients receiving high-dose therapy. Progression-free survival (PFS) was 32.4% and 14.0%, respectively, for the standard-dose and high-dose groups. High-dose treatment led to higher grades of toxicity. The study failed to demonstrate an OS advantage for patients treated with high-dose therapy and hematopoietic stem-cell transplantation (HSCT).

Peinemann et al. (2011) performed a systematic review of the literature related to non-rhabdomyosarcoma soft tissue sarcoma from 54 studies, reporting on 177 participants who received autologous HSCT and 69 who received standard care. Only one study reported comparative data. All studies had a high-risk of bias. Due to a lack of comparative studies the authors noted it is unclear whether participants with non-rhabdomyosarcoma soft tissue sarcomas have improved survival with high-dose chemotherapy and autologous (HSCT).

Verma et al. (2008) performed a systematic review of the literature to determine whether first-line dose-intensive chemotherapy supported by growth factor or autologous bone marrow/stem cell transplantation improves response rate, time-to-disease progression, or survival compared with standard-dose chemotherapy in patients with inoperable, locally advanced, or metastatic soft tissue sarcoma. The authors noted that to date only two RCTs have been performed to determine whether growth factor or autologous bone marrow/stem cell transplantation improves survival, response, or time-to-progression compared with standard-dose chemotherapy in the first-line setting. Only one RCT (n=314) reported data on all three outcomes. No significant difference was noted between treatments for response rate (p=.65). One-year PFS was significantly longer in the high-dose arm (p=.03). This analysis was unable to discern any consistent benefits in patients with metastatic unresectable soft tissue sarcoma when doses higher than standard-dose chemotherapy are used in this setting.

The safety and effectiveness of non-myeloablative or reduced-intensity allogeneic HSCT has also been investigated as treatment for soft tissue sarcoma in adults; however, data from randomized clinical trials are lacking. A well-designed study is required to define the possible role of reduced-intensity stem-cell transplantation for patients with soft tissue sarcoma in whom conventional treatments have failed.

Professional Societies/Organizations
Neither the National Cancer Institute nor the National Comprehensive Cancer Network® has published guidelines regarding the role of HSCT as a treatment option for soft tissue sarcomas in adults.

Summary for Adult Soft Tissue Sarcomas
High-quality randomized clinical trial data are lacking in the published, peer-reviewed scientific literature to demonstrate improved survival with HSCT for this indication. Further professional society/organization support in the form of published consensus guidelines are lacking. The role of HSCT has not yet been established for the treatment of soft tissue sarcomas in adults.

Cancer of the Colon and Rectum: Cancer of the colon and rectum is highly treatable and often curable when localized (National Cancer Institute [NCI], 2012c; NCI, 2012s). Prognosis is related to the degree of penetration of the tumor through the bowel wall and the involvement of lymph nodes.

Literature Review
Non-myeloablative allogeneic HSCT has been investigated for the treatment of colorectal cancer in non-randomized clinical trials (Carnevale-Schianca, 2006; Hentschke, 2003). Trials are limited by small patient populations and study design. Disease progression was common after HSCT; however, data suggest the regression of some metastases associated with graft-versus-host disease (GVHD) is suggestive of a graft-versus-tumor (GVT) effect.

Professional Societies/Organizations
Neither the National Cancer Institute nor the National Comprehensive Cancer Network® has published guidelines regarding the role of HSCT as a treatment option for colorectal cancer.

Summary for Cancer of the Colon and Rectum
Although cancer of the colon and rectum may be responsive to chemotherapy in selected individuals, there is insufficient evidence in the published, peer-reviewed scientific literature in the form of high-quality randomized clinical trials to support the safety and effectiveness of hematopoietic stem-cell transplantation (HSCT) for this indication. Further professional society/organization support as evidenced by published consensus guidelines are lacking. The role of this therapy has not been established for the treatment of colon and/or rectal cancer.

Cancer of the Lung:
Non-Small Cell Lung Cancer (NSCLC): NSCLC is an aggregate of several different types of cells; some of the most common include epidermoid or squamous carcinoma, adenocarcinoma and large cell carcinoma (NCI, 2014k).

Literature Review for NSCLC
The need for more effective therapy has led to the investigation of autologous HSCT in several non-randomized clinical trials involving small patient populations (De Giorgi, 2008; Schilder, 2000; Fetscher, 1997). Response rates were 34%–44% with a median survival of seven to 17 months. It does not appear that high-dose chemotherapy with autologous HSCT improves the response rate or overall survival for patients with NSCLC (Schilder, 2000).

Small Cell Lung Cancer (SCLC): Without treatment, SCLC has the most aggressive course of any type of pulmonary tumor, with a tendency to be more widely disseminated at time of diagnosis. The median survival is two to four months (NCI, 2014s). Compared to other cell types of lung cancer however, SCLC is more responsive to chemoradiation therapies (NCI, 2014s; Chua, 2004). Approximately 50% of patients with limited-disease SCLC receiving standard doses of combination chemotherapy will achieve clinical remission; although remission rates for patients with extensive disease are only 20%–40% (Chua, 2004).

Literature Review for SCLC
Hematopoietic stem-cell transplantation (HSCT) has been studied in multiple prospective randomized and non-randomized clinical trials, and retrospective studies; however, a consistent survival advantage for patients treated with higher doses of chemotherapy has not been demonstrated (Iwasaki, 2005; Elias, 2002; Rizzo, 2002).

Jiang et al. (2009) performed a meta-analysis of five randomized phase II and III clinical trials involving 641 patients with SCLC. The studies compared intensified chemotherapy with hematopoietic progenitors and control therapy, including chemotherapy and radiation. No significant increase in the odds ratio for response was attributed to the use of intensified chemotherapy (p=0.206). No statistically significantly increase in overall survival was found with the use of intensified chemotherapy compared with control regimens (p=0.432). The use

of intensified chemotherapy does not improve outcomes compared with standard therapy in patients with small cell lung cancer.

Professional Societies/Organizations
National Cancer Institute (NCI): The NCI (2014s) notes "The role of dose intensification in patients with small cell lung cancer remains unclear. Early studies showed that under-treatment compromised outcome and suggested that early dose intensification may improve survival. A number of clinical trials have examined the use of colony-stimulating factors to support dose-intensified chemotherapy in SCLC. These studies have yielded conflicting results."

The National Comprehensive Cancer Network® does not mention hematopoietic stem-cell transplantation as a treatment option for NSCLC or SCLC.

Summary for Lung Cancer
Although HSCT is the subject of ongoing research, there is insufficient evidence in the published peer-reviewed scientific literature to support the safety and effectiveness for the treatment of NSCLC or SCLC. Improved complete remission rates and prolonged relapse-free survival rates suggest that this approach is promising; however, the role of HSCT has not yet been established. Several randomized studies are ongoing and should help define whether this approach is of value in this disease.

Epithelial Ovarian Cancer: Ovarian cancer represents tumors of epithelial, germ cell, or sex cord-stromal origin. In general, ovarian tumors are classified according to the kind of cells from which the tumor originated and whether the tumor is benign or cancerous. Identification of the type of cancer is important for treatment and prognosis, as is the stage and grade of tumor. Approximately 90% of ovarian cancer is epithelial in origin and typically occurs in postmenopausal women.

Epithelial ovarian cancer demonstrates a high response rate to standard-dose chemotherapy and several clinical studies have identified a relationship between dose intensity and response. The use of high-dose chemotherapy (HDC) with hematopoietic stem-cell transplantation (HSCT) has been proposed based on the hypothesis that major dose escalations within the myeloablative range are needed to overcome tumor cell resistance and produce a meaningful clinical improvement. However, the use of HSCT remains controversial (Armstrong, 2008; Papadimitriou, 2007). The effectiveness of single or sequential HDC with autologous HSCT has not been proven in several randomized controlled clinical trials (RCT) (Papadimitriou, 2007; Mobus, 2007; Goncalves, 2006; Stiff, 2004), or retrospective comparison of outcomes achieved with HDC compared with standard dose therapy (Stiff, 2000).

Literature Review
Papadimitriou et al. (2007) compared the effectiveness and tolerability of HDC and autologous HSCT as a consolidation approach in women with chemosensitive advanced epithelial ovarian cancer. Eighty patients who achieved their first complete remission after six cycles of standard dose chemotherapy were randomly assigned to receive high-dose melphalan or other treatment. Patients not assigned to the high-dose arm were considered the control arm. Of the 37 patients assigned to receive the high-dose therapy, eleven patients (29%) did not receive high-dose therapy. In an intent-to-treat analysis, there were no significant differences between the two arms in time to progression ($p=0.59$) or overall survival ($p=0.38$). The use of high-dose chemotherapy failed to yield a statistically significant improvement in outcome.

In another RCT involving 58 women with stage III or stage IV persistent or recurrent ovarian cancer, participants were assigned to receive one of two high-dose chemotherapy treatment regimens; both were followed by autologous HSCT. No significant differences were noted in overall or progression-free survival rates between regimens (Stiff, 2004).

In other studies, limited by uncontrolled design and/or small participant populations, high response rates were noted; however, response rates and survival durations were short (Armstrong, 2008; Bengala, 2004; Donato, 2004). Additionally, in a prospective trial by Schilder et al. (2003), individuals with advanced ovarian cancer who had undergone surgical treatment but had not had previous chemotherapy received high-dose chemotherapy (HDC) followed by autologous hematopoietic stem-cell transplantation (HSCT). Complete response rates were low (12.5%); 11 of 45 cycles of the protocol therapy resulted in hospitalizations. High treatment-related morbidity and low efficacy of the therapy did not support continuing, and the study was closed early.

Sequential High-Dose Chemotherapy (HDC) and Autologous HSCT: Sequential cycles of HDC followed by autologous HSCT have also been proposed for the treatment of individuals with stage III and IV epithelial ovarian cancer. Sequential HDC involves performing multiple cycles of chemotherapy followed by a single HSCT. This therapy potentially allows an increase in the total dose of chemotherapy that can be given; however, some patients are unable to tolerate the side effects of the chemotherapy cycle and transplantation process and are therefore unable to complete multiple cycles.

The outcomes achieved in an RCT as well as several case series do not support a clear advantage of sequential HDC and autologous HSCT compared with conventional dose chemotherapy alone (Mobus, 2007; Goncalves, 2006; Ikeba, 2004; Boiko, 2001; Prince, 2001; Schilder, 2001).

Allogeneic HSCT: In theory, the graft-versus-tumor effect from allogeneic HSCT may cause regression of disease in patients with solid tumor cancers; however, there are scarce data in the published, peer-reviewed scientific literature regarding the use of allogeneic HSCT for epithelial ovarian cancer. Studies are limited to small-case series and retrospective analyses. Patient selection has primarily targeted patients with advanced refractory disease who have exhausted all other options, including previous treatment with high-dose chemotherapy with autologous HSCT. Reported outcomes include slow disease regression followed by disease relapse in a majority of patients (Bay, 2010; Donato, 2004; Hanel, 2003).

Professional Societies/Organizations
National Cancer Institute (NCI): The NCI (2014l) notes that high-dose chemotherapy with HSCT support given after initial platinum/paclitaxel induction has not been shown to improve survival in suboptimately cytoreduced stage III or stage IV epithelial ovarian cancer.

National Comprehensive Cancer Network Guidelines™ (NCCN Guidelines™): The NCCN does not mention high-dose chemotherapy with stem-cell transplantation for the treatment of epithelial ovarian cancer, in "Practice Guidelines in Oncology for Ovarian Cancer, Including Fallopian Tube Cancer and Primary Peritoneal Cancer (2014f)".

Summary for Epithelial Ovarian Cancer
To date the effectiveness of single or sequential high-dose chemotherapy followed by autologous or allogeneic HSCT has not been demonstrated by published, peer-reviewed high-quality clinical trial data. Although it remains an area of clinical investigation, the role of this therapy has not yet been established for this indication.

Germ Cell Tumors
Testicular: Highly treatable and frequently curable, ninety percent of testicular cancer is of germ cell origin; two primary types are seminomas, representing 40% of all tumors, and nonseminomas, which represent 60% (American Cancer Society [ACS], 2013). Treatment decisions are based on the type of testicular cancer, stage of disease, and prognostic category. Because the biology of testicular germ cell tumors among adolescents and young adult males differs from tumors arising in infants and young boys, treatment guidelines may not apply to both subgroups (National Cancer Institute [NCI], 2012b).

Standard first-line treatment options may include surgery, standard-dose chemotherapy and/or radiation therapy (NCI, 2012b). For disease that persists despite treatment or has recurred after treatment with standard-dose chemotherapy, prognosis is poor; however, salvage chemotherapy regimens can induce long-term complete responses in about 25% of patients in this treatment group (National Cancer Institute [NCI], 2012b). Because standard dose chemotherapy has limited effect in recurrent disease, salvage therapy with autologous hematopoietic stem-cell transplantation (HSCT) has been proposed.

Ovarian: Malignant germ cell tumors account for approximately 3% to 5% of ovarian malignancies and primarily occur in teens and young adults with a peak age in the early 20s. Tumor types include dysgerminomas, immature teratomas, embryonal tumors, and endodermal sinus (yolk-sac) tumors. Because they are so rare, treatment of malignant germ cell tumors is based largely on the experience with the more common testicular germ cell tumors (Morgan, 2013). Recurrent disease after platinum-based therapy may be salvaged with high-dose chemotherapy and stem-cell rescue (National Comprehensive Cancer Network Guidelines™ [NCCN Guidelines™], 2014f; Morgan, 2013).

Literature Review

Autologous HSCT: The use of autologous HSCT is based on the hypothesis that major dose escalations of chemotherapy within the myeloablative range may overcome tumor cell resistance and produce a meaningful clinical improvement.

Autologous HSCT as Front-Line Therapy: HDC with autologous HSCT has been studied as a front-line treatment for patients with poor-risk testicular cancer; however, randomized (Daugaard, 2011; Droz, 2007, Motzer, 2007) and prospective clinical trials (Miki, 2007) have not demonstrated improved complete response rates or overall survival (OS) when used as initial therapy compared with standard dose chemotherapy. Conventional-dose chemotherapy remains the standard of care for these individuals (Motzer, 2007).

In a phase III randomized controlled trial Daugaard et al. (2011) compared the efficacy of one cycle of standard-dose cisplatin, etoposide, and ifosfamide (VIP) chemotherapy plus three cycles of high-dose VIP chemotherapy followed by autologous HSCT versus four cycles of standard-dose cisplatin, etoposide, and bleomycin (BEP) chemotherapy. One hundred thirty-one individuals with previously untreated metastatic poor-prognosis germ-cell cancer were included in this analysis. The complete response rates (p=0.18) and failure-free survival rates (p=0.060) did not differ between the two treatment arms.

Droz et al. (2007) reported results of a randomized controlled trial (RCT) involving 115 individuals with metastatic nonseminomatous germ cell tumors who received intensified doses of conventional chemotherapy alone (group A), or followed by autologous HSCT (group B) as first-line treatment. There was no statistically significant difference in complete response (57% and 52%, respectively, for groups A and B), or survival rates. The proportion of patients with nonprogressive disease is similar in both groups (75% and 67%, respectively, for groups A and B). According to the authors, the trial failed to demonstrate an impact on response and survival with the use of high-dose therapy and autologous stem-cell support as first-line treatment.

Motzer (2007) reported outcomes of a Phase III prospective, randomized, multicenter trial involving 219 previously untreated male patients with intermediate- or poor-risk germ cell tumor. Patients were randomized to either conventional-dose chemotherapy alone (n=111) or conventional-dose chemotherapy plus HDC and autologous HSCT (n=108). The one-year durable complete response rates were 48% and 52% after conventional chemotherapy and HDC, respectively. There was no difference in survival at 106 months for patients treated with conventional chemotherapy compared with HDC plus autologous HSCT (69% and 68%, respectively).

Autologous HSCT for Relapsed or Refractory Disease: Metastatic testicular tumors that have not been successfully treated by means of initial chemotherapy are potentially curable with salvage chemotherapy (Einhorn, 2007).Use of HDC and autologous HSCT for refractory or relapsed testicular cancer is considered an acceptable treatment option. Durable complete remissions may be achieved with salvage therapy including HDC followed by autologous HSCT in a small percentage of individuals. Improved overall- and disease-free survival rates have been demonstrated in several prospective and retrospective studies (Agawala, 2011; Lorch, 2011; Einhorn, 2007; Lotz, 2005; Schmoll, 2003).

“If the patient experiences an incomplete response or relapses after second line conventional dose chemotherapy, the preferred third-line option would be high-dose chemotherapy with autologous stem cell support (National Comprehensive Cancer Network [NCCN], 2012b).” Published results of case controlled studies show modest improvement with the use of this therapy for relapsed or recurrent disease (Einhorn, 2007; Vaena, 2003).

Although the effectiveness of planned tandem cycles of HDC followed by autologous HSCT has not been proven in randomized controlled clinical trials, it may also be used in the setting of recurrent disease. In a multicenter trial Pico et al. (2005) randomly assigned 280 patients to receive either four cycles of standard dose chemotherapy or three cycles of the same chemotherapy followed by HDC. Complete and partial response rates were similar in both arms (56% and 56%, respectively). No significant improvement in three-year event-free survival was noted with the use of HDC compared with standard-dose (35% versus 42%, respectively). Despite the lack of efficacy data, it has been estimated that 30% of patients with recurrent disease undergo tandem autotransplants (Lazarus, 2007).”

Allogeneic HSCT: There are scarce data in the published, peer-reviewed scientific literature regarding the safety or effectiveness of allogeneic HSCT with myeloablative or non-myeloablative conditioning regimens for the treatment of testicular cancer and the effectiveness of this treatment is unknown.

Professional Societies/Organizations
National Cancer Institute (NCI): Regarding the use of HDC with autologous marrow transplantation for recurrent testicular cancer in adults the NCI (2012b) notes that this therapy "has also been used in uncontrolled case series. However, a randomized controlled trial comparing conventional doses of salvage chemotherapy with HDC with autologous marrow rescue showed more toxic effects and treatment-related deaths in the high-dose arm without any improvement in response rate or overall survival." [

Regarding high-dose chemotherapy (HDC) and hematopoietic stem-cell transplantation (HSCT) for the treatment of recurrent childhood malignant germ cell tumors (GCTs), the NCI (2014a) notes "High dose (HD) chemotherapy with autologous stem cell rescue has been explored in adults with recurrent testicular GCTs. HD chemotherapy plus hematopoietic stem cell rescue has been reported to cure adult patients with relapsed testicular GCTs, even as third-line therapy and in cisplatin-refractory patients. While several other studies support this approach, others do not. Salvage attempts using HD-chemotherapy regimens may be of little benefit if the patient is not clinically disease free at the time of hematopoietic SCT." "The role of HD chemotherapy and hematopoietic stem cell rescue for recurrent pediatric GCTs is not established, despite anecdotal reports. Further study is needed in children and adolescents."

Regarding ovarian germ cell tumors the NCI (2014l) notes "Newer potential treatments include an ifosfamide combination or high-dose chemotherapy and autologous marrow rescue."

The National Comprehensive Cancer Network™ (NCCN™): The NCCN publishes guidelines for the treatment of adults only. Clinical Practice Guidelines in Oncology for Testicular Cancer (2014) note "Prognostic factors can be used in deciding whether a patient is a candidate for conventional dose therapy or high-dose therapy with stem cell support as a second-line option." "Standard second line therapy includes conventional dose chemotherapy or high dose chemotherapy. If the patient experiences an incomplete response or relapses after second line conventional dose chemotherapy, the preferred third-line option would be high-dose chemotherapy with autologous stem cell support or chemotherapy in the context of a clinical trial."

In the Clinical Practice Guidelines in Oncology for Ovarian Cancer (2014f) the NCCN notes high-dose chemotherapy is an acceptable recurrent therapy for malignant germ-cell tumors.

Summary for Germ-Cell Tumors: Several randomized controlled clinical trial data have not demonstrated improved health outcomes with the use of high-dose chemotherapy and autologous HSCT as a front-line therapy. Although data are not robust, the use of single or tandem HDC with autologous HSCT is considered an acceptable therapy for the treatment of individuals with refractory or relapsed testicular and ovarian germ cell tumors.

Renal Cell Carcinoma: Renal cell carcinoma, also known as renal adenocarcinoma, kidney cancer or hypernephroma, is a form of cancer that affects the renal tubules. Approximately 90% of all renal tumors are renal cell carcinoma; 85% of these are clear cell tumors (National Comprehensive Cancer Network Guidelines™ [NCCN Guidelines™], 2013e).

Because of the lack of curative therapy for metastatic disease and the promise of targeted therapies patients should be considered for the many ongoing clinical trials testing single or combination therapies (National Cancer Institute [NCI], 2014r). Hematopoietic stem-cell transplantation (HSCT) has also been proposed as a treatment for renal cell carcinoma.

Autologous HSCT: Data are lacking in the published, peer-reviewed scientific literature regarding the safety and/or effectiveness of autologous HSCT for the treatment of renal cell carcinoma. At this time the role of this therapy has not been established.

Allogeneic HSCT: The NCI (2014r) notes responses to cytotoxic chemotherapy generally have not exceeded 10% for any regimen that has been studied in adequate numbers of patients.

In a retrospective analysis, Nakayama et al. (2007) studied 99 patients with metastatic renal cell carcinoma to characterize the natural history of the disease, identify prognostic factors, and compare outcomes in patients who did (n=23) or did not (n=76) undergo allogeneic HSCT. For those who did not undergo transplantation, patients with poor performance status and brain metastasis were excluded for the purposes of comparison with the transplant group. Overall response rate (i.e. complete and partial response) in the transplant group was 26%; of these, 17% achieved complete response. Treatment-related mortality was 17% and 26% at 100 days and 12 months after transplant, respectively. At a median of seven months, 74% of patients had died in the transplant group. At a median follow-up of 17.4 months, overall survival rates were comparable in the transplant and non-transplant groups (p=.92).

In theory, allogeneic HSCT for solid organ malignancies may induce a graft-versus-tumor reaction. The high treatment-related mortality and suggestion of a graft-versus-tumor effect associated with myeloablative preparative regimens has led to the study of reduced-intensity and non-myeloablative preparative regimens as conditioning for allogeneic stem-cell transplantation. In several nonrandomized case series and retrospective analyses with small patient populations, complete donor chimerism was observed in the majority of patients. Response rates were variable at 0%−42%. Despite reduced intensity or non-myeloablative conditioning, treatment-related mortality rates are 12%–33%, primarily from graft-versus-host disease (Bregni, 2009; Peres, 2007; Yun, 2007; Barkholt, 2006; Artz, 2005; Massenkeil, 2004; Bregni, 2002; Rini, 2002; Childs, 2000). One-year survival rates are 18%–59%; there are scarce data regarding long-term outcomes.

Professional Societies/Organizations
Neither the National Cancer Institute nor the National Comprehensive Cancer Network® has published guidelines regarding the role of HSCT as a treatment option for renal cell carcinoma.

Summary for Renal Cell Carcinoma
High treatment-related toxicity remains an obstacle to the safety and effectiveness of HSCT for renal cell carcinoma. Optimal patient selection criteria, most effective conditioning regimen, and strategies to exploit the graft-versus-tumor effect continue to be identified. While promising, there is insufficient evidence to demonstrate the safety and effectiveness of allogeneic HSCT for this indication. The role of this therapy has not yet been established for renal cell carcinoma.

Other Solid Tumors: There are scarce data in the published peer-reviewed scientific literature to support the safety and effectiveness of autologous or allogeneic HSCT for the treatment of other adult soft tumors including, but not limited to, cancers of the bile duct, cervix, esophagus, gallbladder, melanoma, nasopharynx, pancreas, paranasal sinus, prostate, stomach (gastric cancer), thymus, thyroid, or uterus.

Professional Societies/Organizations
Neither the National Cancer Institute nor the National Comprehensive Cancer Network® has published guidelines regarding the role of HSCT as a treatment option for these indications.

Summary for Other Cancers
High-quality published peer-reviewed clinical trial data are lacking to support the safety and effectiveness of HSCT for the treatment of any of these indications. Further there is a lack of professional society/organization support in the form of published consensus guidelines for the use of HSCT. At this time the role of HSCT has not been established.

Use Outside of the US:
Cancer Care Ontario: On behalf of the Sarcoma Disease Site Group of Cancer Care Ontario's Program in Evidence-Based Care, Verma et al. (2008) published a clinical practice guideline for Dose-Intensive Chemotherapy with Growth Factor or Autologous Bone Marrow or Stem-Cell Transplant Support in First-Line Treatment of Advanced or Metastatic Adult Soft Tissue Sarcoma. The recommendations note:

- Dose-intensive chemotherapy with growth factor support is not recommended in the first-line treatment of patients with inoperable locally advanced or metastatic soft tissue sarcoma.
- The data are insufficient to support the use of high dose chemotherapy with autologous bone marrow or stem-cell transplantation as first-line treatment in this group of patients.
- Eligible patients should be encouraged to enter clinical trials assessing novel approaches or compounds.

Summary
Published clinical trial data have established the effectiveness of hematopoietic stem-cell transplantation (HSCT) as treatment for testicular and ovarian germ cell tumors. Likewise, professional census guidelines support the use of HSCT as a treatment option to improve health outcomes.

Although many solid tumors occurring in adults are chemo-or radiosensitive results may not be durable; HSCT has been proposed as a means to intensify chemotherapy dosage in other solid tumors. However, at this time there are limited high-quality clinical trial data to support the safety and effectiveness of this therapy to improve health outcomes for these indications as noted in the Coverage Policy.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Autologous

Covered when medically necessary when used to report autologous bone marrow or blood-derived stem cell procedures for the treatment of testicular and ovarian germ cell tumors

CPT®* Codes	Description
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
38211	Transplant preparation of hematopoietic progenitor cells; tumor cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38232	Bone marrow harvesting for transplantation; autologous
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

HCPCS Codes	Description
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including: pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days or pre-and post-transplant care in the global definition

Experimental/Investigational/Unproven/Not Covered when used to report allogeneic bone marrow or blood-derived stem cell procedures for the treatment of testicular cancer:

CPT* Codes	Description
38205	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; allogeneic
38207	Transplant preparation of hematopoietic progenitor cells; cryopreservation and

	storage
38208	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, without washing, per donor
38209	Transplant preparation of hematopoietic progenitor cells; thawing of previously frozen harvest, with washing, per donor
38210	Transplant preparation of hematopoietic progenitor cells; specific cell depletion within harvest, T-cell depletion
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal
38213	Transplant preparation of hematopoietic progenitor cells; platelet depletion
38214	Transplant preparation of hematopoietic progenitor cells; plasma (volume) depletion
38215	Transplant preparation of hematopoietic progenitor cells ; cell concentration in plasma, mononuclear, or buffy coat layer
38230	Bone marrow harvesting for transplantation, allogeneic
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation, per donor
38242	Allogeneic lymphocyte infusions

HCPCS Codes	**Description**
S2140	Cord blood harvesting for transplantation, allogeneic
S2142	Cord blood-derived stem-cell transplantation, allogeneic
S2150	Bone marrow or blood-derived stem cells (peripheral or umbilical), allogeneic or autologous, harvesting, transplantation, and related complications; including: pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days or pre-and post-transplant care in the global definition

References

1. Agawala AK, Perkins SM, Abonour R, Brames MJ, Einhorn LH. Salvage chemotherapy with high-dose carboplatin and etoposide with peripheral blood stem cell transplant in patients with relapsed pure seminoma. Am J Clin Oncol. 2011 Jun;34(3):286-8.

2. Albers P, Albrecht W, Algaba F, Bokemeyer C, Cohn-Cedermark G, Horwich A, et al. Guidelines on testicular cancer. Eur Urol. 2005 Dec;48(6):885-94. Epub 2005 Jul 18.

3. American Cancer Society. Detailed Guide: What is cervical cancer? Updated 2014 Jan 31. Accessed March 14, 2014 (a). Available at URL address: http://www.cancer.org/docroot/CRI/content/CRI_2_4_1X_What_is_cervical_cancer_8.asp?sitearea=

4. American Cancer Society. Detailed Guide: Kidney cancer (adult)-renal cell carcinoma. (b) Updated 2013 Jan 18. Accessed March 14, 2014. Available at URL address: http://www.cancer.org/docroot/CRI/CRI_2_3x.asp?dt=22

5. American Cancer Society Detailed Guide: What is non-small cell lung cancer? (c) Updated 2014 Feb 10. Accessed March 14, 2014. Available at URL address: http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/index

6. American Cancer Society Detailed Guide: What is small cell lung cancer? (d) Updated 2014 Feb 11. Accessed March 14, 2014. Available at URL address: http://www.cancer.org/Cancer/LungCancer-SmallCell/DetailedGuide/index

7. American Cancer Society. Detailed Guide: What is thymus cancer? (e) Updated 2014 Feb 11. Accessed March 14, 2014. Available at URL address: http://www.cancer.org/Cancer/ThymusCancer/DetailedGuide/index

8. American Cancer Society. Ovarian cancer. (f) Updated 2014 Feb 6. Accessed Mar 14, 2014. Available at URL address: http://documents.cancer.org/114.00/114.00.pdf

9. American Cancer Society. Testicular cancer. (g) Updated 2014 Feb 11. Accessed March 14, 2014. Available at URL address: http://documents.cancer.org/121.00/121.00.pdf

10. Artz AS, van Besien K, Zimmerman T, Gajewski TF, Rini BL, Hu HS, et al. Long-term follow-up of nonmyeloablative allogeneic stem cell transplantation for renal cell carcinoma: The University of Chicago Experience. Bone Marrow Transplant. 2005 Feb;35(3):253-60.

11. Arya M, Chao D, Patel H. Allogeneic hematopoietic stem-cell transplantation: the next generation of therapy for metastatic renal cell cancer. Nature Clinical Practice Oncology. 2004 Nov;1(1):32-8.

12. Barkholt L, Bregni M, Remberger M, Blaise D, Peccatori J, Massenkeil G, et al. Allogeneic haematopoietic stem cell transplantation for metastatic renal carcinoma in Europe. Ann Oncol. 2006 Jul;17(7):1134-40. Epub 2006 Apr 28.

13. Bay O, Cabrespine-Faugeres A, Tabrizi R, Blaise D, Viens P, Ehninger G, et al. Allogeneic hematopoietic stem cell transplantation in ovarian cancer-the EBMT experience. Int J Cancer. 2010 Sep 1;127(6):1446-52.

14. Bengala C, Guarneri V, Ledermann J, Rosti G, Wandt H, Lotz J-P, et al. High-dose chemotherapy with autologous haemopoietic support for advanced ovarian cancer in first complete remission: retrospective analysis from the solid tumour registry of the European Group for Blood and Marrow Transplantation (EBMT). Bone Marrow Transplant. 2004;36:25-31.

15. Bhatia S, Abonour R, Porcu P, Seshadri R, Nichols CR, Cornetta K, et al. High-dose chemotherapy as initial salvage chemotherapy in patients with relapsed testicular cancer. J Clin Oncol. 2000 Oct 1;18(19):3346-51.

16. Blaise D, Bay JO, Faucher C, Michallet M, Boiron JM, Choufi B, et al. Reduced-intensity preparative regimen and allogeneic stem cell transplantation for advanced solid tumors. Blood. 2004 Jan 1;103(2):435-41.

17. Bojko P, Scheulen ME, Hilger R, Oberhoff C, Schindler AE, Seeber S. High-dose chemotherapy with peripheral blood stem cell transplantation for patients with advanced ovarian cancer. J Cancer Res Clin Oncol. 2001;127:243-50.

18. Bosl GJ, Feldman DR, Bajorin DF, Sheinfeld J, Motzer RJ, Reuter VE, et al. Cancer of the testis. In: DeVita, Jr. VT, Lawrence TS, Rosenberg SA, editors. DeVita, Hellman and Rosenberg's Cancer: Principles & Practice of Oncology, 9th ed., Philadelphia: Lippincott Williams & Wilkins; 2011.

19. Bregni M, Bernardi M, Servida P, Pescorollo A, Crocchiolo R, Treppiedi E, et al. Long-term follow-up of metastatic renal cancer patients undergoing reduced-intensity allografting. Bone Marrow Transplant. 2009 Aug;44(4):237-42.

20. Bregni M, Dodero A, Peccatori J, Pescarollo A, Bernardi M, Sassi I, et al. Nonmyeloablative conditioning followed by hematopoietic cell allografting and donor lymphocyte infusions for patients with metastatic renal and breast cancer. Blood. 2002 Jun 1;99(11):4234-6.

21. Bregni M, Herr W, Blaise D, Allogeneic stem cell transplantation for renal cell carcinoma. Solid Tumor Working Party of EBMT. Expert Rev Anticancer Ther. 2011 Jun;11(6):901-11.

22. Bucholz E, Manegold C, Pilz L, Thatcher N, Drings P. Standard versus dose-intensified chemotherapy with sequential reinfusion of hemapoietic progenitor cells in small cell lung cancer patients with favorable prognosis. J Thorac Oncol. 2007 Jan;2(1):51-8.

23. Bui-Nguyen B, Ray-Coquard I, Chevreau C, Penel N, Bay JO, Coindre JM, et al. High-dose chemotherapy consolidation for chemosensitive advanced soft tissue sarcoma patients: an open-label, randomized controlled trial. Ann Oncol. 2012 Mar;23(3):777-84.

24. Busca A, Novarino A, de Fabritiis P, Picardi A, Zeuli M, Locatelli F, et al. Nonmyeloablative allogeneic blood stem cell transplantation in patients with metastatic solid tumors. Hematology. 2006 Jun;11(3):171-7.

25. Cannistra SA, Gershenson DM, Recht A. Ovarian cancer, fallopian tube carcinoma, and peritoneal carcinoma. In: DeVita, Jr. VT, Lawrence TS, Rosenberg SA, editors. Devita, Hellman, & Rosenberg's Cancer: principles & practice of oncology, 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.

26. Carnevale-Schianca F, Cignetti A, Capaldi A, Vitaggio K, Vallario A, Ricchiardi A, et al. Allogeneic nonmyeloablative hematopoietic cell transplantation in metastatic colon cancer: tumor-specific T cells directed to a tumor-associated antigen are generated in vivo during GVHD. Blood. 2006 May 1;107(9):3795-803. Epub 2006 Jan 10.

27. Castermans E, Baron F, Willems E, Schaaf-Lafontaine N, Meuris N, Gothot A, et al. Evidence for neo-generation of T-cells by the thymus after non-myeloablative conditioning. Haematologica. 2008 Feb;93(2):240-47.

28. Chen TY, Chen HH, Su WC, Tsao TJ. High-dose chemotherapy and hematopoietic stem cell transplantation for patients with nasopharyngeal cancer: a feasibility study. Jpn J Clin Oncol. 2003 Jul;33(7):331-5.

29. Childs RW. Allogeneic stem cell transplantation. In: DeVita VT, Lawrence TS, Rosenberg SA, editors. DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology. 9th ed. Philadelphia: Lippincott, Williams and Wilkins;2011.

30. Childs R, Chernoff A, Contentin N, Bahceci E, Schrump D, Leitman S, et al. Regression of metastatic renal-cell carcinoma after nonmyeloablative allogeneic peripheral-blood stem-cell transplantation. N Engl J Med. 2000 Sep 14;343(11):750-8.

31. Chua YJ, Steer C, Yip D. Recent advances in management of small-cell lung cancer. Cancer Treat Rev. 2004 Oct;30(6):521-43.

32. Conrad R, Remberger M, Cederlund K, Ringden O, Barkholt L. A comparison between low intensity and reduced intensity conditioning in allogeneic hematopoietic stem cell transplantation for solid tumors. Haematologica. 2008 Feb;93(2):265-72.

33. Daugaard G, Skoneczna I, Aass N, De Wit R, De Santis M, Dumez H, et al. A randomized phase III study comparing standard dose BEP with sequential high-dose cisplatin, etoposide, and ifosfamide (VIP) plus stem-cell support in males with poor-prognosis germ-cell cancer. An intergroup study of EORTC, GTCSG, and Gruppo Germinal (EORTC 30974). Ann Oncol. 2011 May;22(5):1054-61.

34. De Giorgi U, Blaise D, Lange A, Viens P, Marangolo M, Madroszyk A, et al. High-dose chemotherapy with peripheral blood progenitor cell support for patients with non-small cell lung cancer: the experience of the European Group for Bone Marrow Transplantation (EBMT) Solid Tumors Working Party. Bone Marrow Transplant. 2007 Dec;40(11):1045-8. Epub 2007 Oct 8.

35. Demirer T, Barkholt L, Blaise D, Pedrazzoli P, Aglietta M, Carella AM, et al. Transplantation of allogeneic hematopoietic stem cells: an emerging treatment modality for solid tumors. Nat Clin Pract Oncol. 2008 May;5(5):256-67. Epub 2008 Apr 8.

36. Donato ML, Aleman A, Champlin RE, Saliba RM, Wharton JT, Burke TW, et al. Ovarian Cancer: analysis of 96 patients with advanced ovarian carcinoma treated with high-dose chemotherapy and autologous stem cell transplantation. Bone Marrow Transplant. (a) 2004;33:1219-1224.

37. Donato ML, Levenback C, Gershenson DM, McMeekin S, Champlin RE. Matched unrelated donor bone marrow transplantation for the treatment of platinum refractory ovarian carcinoma: a case report. Gynecol Oncol. (b) 2004;97:365-7.

38. Droz JP, Kramar A, Biron P, Pico JL, Kerbrat P, Peny J, et al. Failure of high-dose cyclophosphamide and etoposide combined with double-dose cisplatin and bone marrow support in patients with high-volume metastatic nonseminomatous germ-cell tumours: mature results of a randomized trial. Eur Urol. 2007 Mar;51(3):739-46.

39. ECRI Institute. Allogeneic stem cell transplantation for treatment of metastatic renal cell carcinoma. [Emerging Technology evidence report]. Plymouth Meeting (PA): ECRI Institute; 2001 Nov. Available at URL address: www.ecri.com

40. ECRI Institute. High-dose chemotherapy with autologous bone marrow or peripheral stem cell transplant for epithelial ovarian cancer. Plymouth Meeting (PA): ECRI Institute Health Technology Assessment Information Service; 2004 Dec. 57 p. (Evidence Report; no. 117). Available at URL address: www.ecri.org.

41. Einhorn HL, Williams SD, Chamness A, Brames MJ, Perkins SM, Abonour R. High-dose chemotherapy and stem-cell rescue for metastatic germ-cell tumors. N Engl J Med. 2007 Jul 26;357(4):340-8.

42. El-Helw L, Coleman RE. Anti-tumour treatment: salvage, dose intense and high-dose chemotherapy for the treatment of poor prognosis or recurrent germ cell tumours. Cancer Treat Rev. 2005 (31);197-209.

43. Elias AD, Skarin AT, Richardson P, Ibrahim J, McCauley M, Frie E. Dose-intensive therapy for extensive-stage small cell lung cancer and extrapulmonary small cell carcinoma: long-term outcome. Biol Blood Marrow Transplant. 2002;8(6):326-33.

44. Engelhardt M, Zeiser R, Ihorst G, Finke J, Muller CI. High-dose chemotherapy and autologous peripheral blood stem cell transplantation in adult patients with high-risk or advanced Ewing and soft tissue sarcoma. J Cancer Res Clin Oncol. 2007 Jan;133(1):1-11. Epub 2006 Jul 12.

45. Ferrandina G, Perillo A, Distefano M, D'Agostino G, Gallotta V, Pierelli L, et al. Carboplatin-based neoadjuvant treatment with peripheral blood stem cell and growth factor support in locally advanced cervical cancer patients with bulky metastatic lymph nodes. Eur J Obstet Gynecol Reprod Biol. 2007 Apr;131(2):236-8. Epub 2006 May 2.

46. Fetscher S. The role of high-dose chemotherapy in the treatment of non-small cell lung cancer. Crit Rev Oncol Hematol. 2002 Feb;41(2):151-6.

47. Fetscher S, Brugger W, Engelhardt R, Kanz L, Hasse J, Frommhold H, et al. Dose-intense therapy with etoposide, ifosfamide, cisplatin, and epirubicin (VIP-E) in 107 consecutive patients with limited- and extensive-stage non-small cell lung cancer. Ann Oncol. 1997 Jan;8(1):57-64.

48. Goncalves A, Delva R, Fabbro M, Gladeiff L, Lotz JP, Ferrero JM, et al. Post-operative sequential high-dose chemotherapy with haematopoietic stem cell support as front-line treatment in advanced ovarian cancer: a phase II multicentre study. Bone Marrow Transplant. 2006 Apr;37(7):651-9.

49. Goodwin A, Gurney H, Gottlieb D. Allogeneic bone marrow transplant for refractory mediastinal germ cell tumour: possible evidence of graft-versus-tumour effect. Intern Med J. 2007 Feb;37(2):127-9.

50. Gratwohl A, Baldomero H, Demirer T, Rosti G, Dini G, Ladenstein R, et al. Hematopoetic stem cell transplantation for solid tumors in Europe. Ann Oncol. 2004 Apr;15(4):653-60.

51. Hanel M, Bornhauser M, Muller J, Thiede C, Ehninger G, Kroschinsky F. Evidence for a graft-versus-tumor effect in refractory ovarian cancer. J Cancer Res Clin Oncol. 2003;129:12-6.

52. Hanna N, Gharpure VS, Abonour R, Cornetta K, Loehrer PJ Sr. High-dose carboplatin with etoposide in patients with recurrent thymoma: the Indiana University experience. Bone Marrow Transplant. 2001 Sep;28(5):435-8.

53. Hara I, Miyake H, Yamada Y, Yamanaka K, Furukawa J, Kumano M, et al. Feasibility and usefulness of high-dose chemotherapy (high-dose ifosfamide, carboplatin and etoposide) combined with peripheral blood stem cell transplantation for male germ cell tumor: a single-institute experience. Anticancer Drugs. 2006 Oct;17(9):1057-66.

54. Hartmann J, Einhorn L, Nichols CR, Droz JP, Horwich A, Gerl A, et al. Second-line chemotherapy in patients with relapsed extragonadal nonseminomatous germ cell tumors: results of an international multicenter analysis. J Clin Oncol. 2001 Mar 15;19(6):1641-8.

55. Hentschke P, Barkholt L, Uzunel M, Mattsson J, Wersall P, Pisa P, et al. Low-intensity conditioning and hematopoietic stem cell transplantation in patients with renal and colon carcinoma. Bone Marrow Transplant. 2003 Feb;31(4):253-61.

56. Humblet Y, Symann M, Bosly A, Delaunois L, Francis C, Machiels J, et al. Late intensification chemotherapy with autologous bone marrow transplantation in selected small-cell carcinoma of the lung: a randomized study. J Clin Oncol. 1987 Dec;5(12):1864-73.

57. Ikeba K, Okubo M, Takeda S, Kinoshita K, Maeda H. Five-year results of cyclic semi-high dose neoadjuvant chemotherapy supported by autologous peripheral blood stem-cell transplantation in patients with advanced ovarian cancer. Int J Clin Oncol. 2004;9:113-9.

58. Iwasaki Y, Nagata K, Nakanishi M, Natuhara A, Kubota Y, Ueda M, et al. Double-cycle, high-dose ifosfamide, carboplatin, and etoposide followed by peripheral blood stem-cell transplantation for small cell lung cancer. Chest. 2005 Oct;128(4):2268-73.

59. Iwasaki Y, Ohsugi S, Takemura Y, Nagata K, Harada H, Nakagawa M. Multidisciplinary therapy including high-dose chemotherapy followed by peripheral blood stem cell transplantation for invasive thymoma. Chest 2002 Dec;122(6):2249-52.

60. Jiang J, Shi HZ, Deng JM, Liang QL, Qim SM, Wu C. Efficacy of intensified chemotherapy with hematopoietic progenitors in small-cell lung cancer: A meta-analysis of the published literature. Lung Cancer. 2009 Aug;65(2):214-8.

61. Jones RH, Vasey PA. Part I: testicular cancer: management of early disease. Lancet Oncol. 2003 Dec;4:730-7.

62. Jones RH, Vasey PA. Part II: testicular cancer: management of advanced disease. Lancet Oncol. 2003 Dec;4:738-47.

63. Kanda Y, Komatsu Y, Akahane M, Kojima S, Asano-Mori Y, Tada M, et al. Graft-versus-tumor effect against advanced pancreatic cancer after allogeneic reduced-intensity stem cell transplantation. Transplantation. 2005 Apr 15;79(7):821-7.

64. Kanda Y, Omuro Y, Baba E, Oshima K, Nagafuji K, Heike Y, et al. Allo-SCT using reduced-intensity conditioning against advanced pancreatic cancer: a Japanese survey. Bone Marrow Transplant. 2008 Jul;42(2):99-103. Epub 2008 Apr 7.

65. Kasper B, Scharrenbroich I, Schmidt T, Wuchter P, Dietrich S, Ho AD, et al. Consolidation with high-dose chemotherapy and stem-cell support for responding patients with metastatic soft tissue sarcomas: prospective single-institutional phase II study. Bone Marrow Transplant. 2010 Jul;45(7):1234-8.

66. Kaufman J, Horn L., Carbone D. Molecular Biology of Lung Cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, editors. Cancer: Principles and Practice of Oncology. 9th ed. Philadelphia: Lippincott, Williams and Wilkins;2011.

67. Krege S, Beyer J, Souchon R, Albers P, Albrecht W, Algaba F, et al. European Consensus Conference on diagnosis and treatment of germ cell cancer: a report of the second meeting of the European Germ Cell Cancer Consensus Group (EGCCCG): Part II. European Urology. 2008;53: 497-513.

68. Lazarus HM, Stiff PJ, Carrerus J, Logan BR, Akard L, Bolwell BJ, et al. Utility of single versus tandem autotransplants for advanced testes/germ cell cancer: a center for international blood and marrow transplant research (CIBMTR) analysis. Biol Blood Marrow Transplant. 2007 Jul;13(7):778-89. Epub 2007 Apr 30.

69. Linehan WM, Rini BI, Yang JC. Cancer of the kidney. DeVita VT, Lawrence TS, Rosenberg SA, editors. In: DeVita, Hellman, and Rosenberg's Cancer: principles and practice of oncology. 9th ed. Philadelphia (PA): Lippincott, Williams & Wilkins; 2011

70. Lorch A, Bascoul-Mollevi C, Kramar A, Einhorn L, Necchi A, Massard C, et al. Conventional-dose versus high-dose chemotherapy as first salvage treatment in male patients with metastatic germ cell tumors: evidence from a large international database. J Clin Oncol. 2011 Jun 1;29(16):2178-84.

71. Lorigan P, Woll PJ, O'Brien ME, Ashcroft LF, Sampson MR, Thatcher N. Randomized phase III trial of dose dense chemotherapy supported by whole-blood hematopoietic progenitors in better prognosis small-cell lung cancer. J Natl Cancer Inst. 2005 May 4;97(9):667-74.

72. Lotz J-P, Bui B, Gomez F, Theodore C, Caty A, Fizazi K, et al. Sequential high-dose chemotherapy protocol for relapsed poor prognosis germ cell tumors combining two mobilization and cytoreductive treatments followed by three high-dose chemotherapy regimens supported by autologous stem cell transplantation: results of the phase II multicentric TAXIF trial. Ann of Oncol. 2005;(16) 411-418.

73. Markman M, Walker JL. Intraperitoneal chemotherapy of ovarian cancer: a review, with a focus on practical aspects of treatment. J Clin Oncol. 2006 Feb 20;24(6)1-7.

74. Massenkeil G, Roigas J, Nagy M, Wille A, Stroszczynski C, Mapara MY, et al. Nonmyeloablative stem cell transplantation in metastatic renal cell carcinoma: delayed graft-versus-tumor effect is associated with chimerism conversion but transplantation has high toxicity. Bone Marrow Transplant. 2004 Aug;34(4):309-16.

75. Meisenberg BR, Ross M, Vredenburg JJ, Jones R, Shpall EJ, Siegler HF, et al. Randomized trial of high-dose chemotherapy with autologous bone marrow support as adjuvant therapy for high-risk, multi-node-positive malignant melanoma. J Natl Cancer Inst. 1993 Jul 7;85(13):1080-5.

76. Miki T, Mizutani Y, Akaza H, Ozono S, Tsukamoto T, Terachi T, et al. Long-term results of first-line sequential high-dose carboplatin, etoposide and ifosfamide chemotherapy with peripheral blood stem cell support for patients with advanced testicular germ cell tumor. Int J Urol. 2007 Jan;14(1):54-9.

77. Mobus V, Wandt H, Frickhofen N, Bengala C, Champion K, Kimmig R, et al. Phase III trial of high-dose sequential chemotherapy with peripheral blood stem cell support compared with standard dose chemotherapy for first-line treatment of advanced ovarian cancer: intergroup trial of the AGO-Ovar/AIO and EBMT. J Clin Oncol. 2007 Sep 20;25(27):4187-93. Epub 2007 Aug 13.

78. Morgan M, Boyd J, Drapin R, Seiden MV. Cancers arising in the ovary. In: Niederhuber JE, Armitage JO, Doroshow JH , Kastan MB, Tepper JE, editors. Abeloff's clinical oncology, 5th ed. New York: Churchill Livingstone; 2013.

79. Motzer RJ, Nichols CJ, Margolin KA, Bacik J, Richardson PG, Vogelzang NJ, et al. Phase III randomized trial of conventional-dose chemotherapy with or without high-dose chemotherapy and

autologous hematopoietic stem-cell rescue as first-line treatment for patients with poor-prognosis metastatic germ cell tumors. J Clin Oncol. 2007 Jan 20;25(3):247-56.

80. Nakayama K, Tannir MN, Liu P, Wathen JK, Cheng YC, Champlin RE, et al. Natural history of metastatic renal cell carcinoma in patients who underwent consultation for allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2007 Aug;13(8):975-85.

81. Nath SV, Prince HM, Choong PF, Toner GC. Durable remissions are rare following high dose therapy with autologous stem cell transplantation for adults with "paediatric" bone and soft tissue sarcomas. Int Semin Surg Oncol. 2005 May 31;2(1):12.

82. National Cancer Institute (a). Adult soft tissue sarcoma treatment (PDQ®). Health professional version. Updated 2014 Feb 28. Accessed March 15, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/adult-soft-tissue-sarcoma/healthprofessional/allpages

83. National Cancer Institute (b). Cervical cancer treatment (PDQ®). Health professional version. Updated 2014 March 14. Accessed March 15, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/cervical/HealthProfessional/page1

84. National Cancer Institute. Childhood extracranial germ cell tumor treatment (PDQ®). [Health professional version] [c.] Updated 2014 Jan 27. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/extracranial-germ-cell/HealthProfessional/page7

85. National Cancer Institute (a). Colon cancer treatment (PDQ®). Health professional version. Updated 2013 Feb 8. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/colon/healthprofessional

86. National Cancer Institute (d). Endometrial cancer treatment (PDQ®). Health professional version. Updated 2014 March 14. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/endometrial/healthprofessional

87. National Cancer Institute (e). Esophageal cancer treatment (PDQ®). Health professional version. Updated 2014 March 13. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/esophageal/healthprofessional

88. National Cancer Institute (f). Extrahepatic bile duct cancer treatment (PDQ®). Health professional version. Updated 2014 March 13. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/bileduct/HealthProfessional

89. National Cancer Institute (g). Gallbladder cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 28. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/gallbladder/healthprofessional

90. National Cancer Institute (h). Gastric cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 27. Accessed March 10, 2104. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/gastric/HealthProfessional

91. National Cancer Institute (i). Gastrointestinal carcinoid tumors treatment (PDQ®). Health professional version. Updated 2014 Feb 28. Accessed March 10, 2104. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/gastrointestinalcarcinoid/HealthProfessional/page1

92. National Cancer Institute (j). Hypopharyngeal cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 28. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/hypopharyngeal/HealthProfessional/page1

93. National Cancer Institute (b). Melanoma treatment (PDQ®). Health professional version. Updated 2013 May 16. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/melanoma/healthprofessional

94. National Cancer Institute (a). Nasopharyngeal cancer treatment (PDQ®). Health professional version. Updated 2012 Oct 12. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/nasopharyngeal/healthprofessional

95. National Cancer Institute (k). Non-small cell lung cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 21. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/healthprofessional

96. National Cancer Institute (NCI). (l) Ovarian epithelial cancer treatment (PDQ®): Health professional version. Updated 2014 Jan 31. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/ovarianepithelial/healthprofessional

97. National Cancer Institute (m). Pancreatic cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 21. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/pancreatic/healthprofessional

98. National Cancer Institute (n). Pancreatic neuroendocrine tumors (islet cell tumors) Treatment (PDQ®). Health professional version. Updated 2014 March 7. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/isletcell/healthprofessional

99. National Cancer Institute (o). Paranasal sinus and nasal cavity cancer treatment (PDQ®). Health professional version. Updated 2014 March 7. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/paranasalsinus/HealthProfessional

100. National Cancer Institute (p). Prostate cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 14. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/prostate/healthprofessional

101. National Cancer Institute (q). Rectal cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 8. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/rectal/healthprofessional

102. National Cancer Institute (NCI). (r) Renal cell carcinoma treatment (PDQ®) [health professional version]. Updated 2014 Feb 21. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/renalcell/healthprofessional

103. National Cancer Institute (s). Small cell lung cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 21. Accessed Jan 3, 2013. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/small-cell-lung/healthprofessional

104. National Cancer Institute (b). Testicular cancer treatment (PDQ®) [Health professional version]. Updated 2012 Jan 20. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/testicular/healthprofessional

105. National Cancer Institute (t). Thymoma and thymic carcinoma treatment (PDQ®). Health professional version. Updated 2014 March 12. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/thymoma/healthprofessional

106. National Cancer Institute (u). Thyroid cancer treatment (PDQ®). Health professional version. Updated 2014 Feb 28. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/thyroid/healthprofessional

107. National Cancer Institute. (c) Uterine sarcoma treatment (PDQ®). Health professional version. Updated 2012 Oct 18. Accessed March 10, 2014. Available at URL address: http://www.cancer.gov/cancertopics/pdq/treatment/uterinesarcoma/healthprofessional

108. National Comprehensive Cancer Network® (NCCN) [a]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Anal carcinoma. V2.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/anal.pdf

109. National Comprehensive Cancer Network® (NCCN) [a]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Cervical cancer. V1.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf

110. National Comprehensive Cancer Network® (NCCN) [b]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Colon cancer. V3.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf

111. National Comprehensive Cancer Network® (NCCN) [b]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Esophageal and esophagogastric junction cancers (excluding the proximal 5cm of the stomach). V2.2013. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf

112. National Comprehensive Cancer Network® (NCCN) [c]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Gastric cancer (including cancer in the proximal 5 cm of the stomach). V2.2013. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/gastric.pdf

113. National Comprehensive Cancer Network® (NCCN) [d]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Head and neck cancers. V2.2013. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf

114. National Comprehensive Cancer Network® (NCCN) [c]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Hepatobiliary cancers. V1.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf

115. National Comprehensive Cancer Network® (NCCN). [e] NCCN GUIDELINES™ Clinical Guidelines in Oncology™. Kidney cancer. V2.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf

116. National Comprehensive Cancer Network® (NCCN) [d]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Melanoma. V3.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/melanoma.pdf

117. National Comprehensive Cancer Network® (NCCN) [f]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Neuroendocrine tumors. V2.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/neuroendocrine.pdf

118. National Comprehensive Cancer Network® (NCCN) [e]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Non-small-cell lung cancer. V3.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf

119. National Comprehensive Cancer Network® (NCCN). [f] NCCN GUIDELINES™ Clinical Guidelines in Oncology™. Ovarian cancer including fallopian tube cancer and primary peritoneal cancer. V.1.2014. ©

National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/ovarian.pdf

120. National Comprehensive Cancer Network® (NCCN) [g]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Pancreatic adenocarcinoma. V1.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/pancreatic.pdf

121. National Comprehensive Cancer Network® (NCCN) [e]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Prostate cancer. V1.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf

122. National Comprehensive Cancer Network® (NCCN) [h]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Rectal cancer. V3.2014. © National Comprehensive Cancer Network, Inc. 2014, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/rectal.pdf

123. National Comprehensive Cancer Network® (NCCN) [f]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Small cell lung cancer. V2.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/sclc.pdf

124. National Comprehensive Cancer Network® (NCCN). [g] NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Testicular cancer. V1.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/testicular.pdf

125. National Comprehensive Cancer Network® (NCCN) [h]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Thyroid carcinoma. V2.2013. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/thyroid.pdf

126. National Comprehensive Cancer Network® (NCCN) [i]. NCCN GUIDELINES™ Clinical Guidelines in Oncology ™. Uterine neoplasms. V1.2014. © National Comprehensive Cancer Network, Inc. 2013, All Rights Reserved. Accessed March 10, 2014. Available at URL address: http://www.nccn.org/professionals/physician_gls/PDF/uterine.pdf

127. National Institutes of Health (NIH). Renal cell carcinoma. Copyright 1997-2014. Updated 2013 March 4. Accessed March 10, 2014. Available at URL address: http://www.nlm.nih.gov/medlineplus/ency/article/000516.htm

128. Numata A, Yasuda K, Fukuda T, Baba E, Yamasaki S, Takase K, et al. Non-myeloablative allogeneic haemopoietic stem-cell transplantation for treatment of metastatic invasive thymoma. Lancet Oncol. 2005 Aug;6(8):626-8.

129. O'Sullivan JM, McCready VR, Flux G, Norman AR, Buffa FM, Chittenden S, et al. High activity Rhenium-186 HEDP with autologous peripheral blood stem cell rescue: a phase I study in progressive hormone refractory prostate cancer metastatic to bone. Br J cancer.2002 Jun 5;86(11):1715-20.

130. O'Sullivan JM, Norman AR, McCready VR, Flux G, Buffa FM, Johnson B, et al. A phase 2 study of high-activity 186Re-HEDP with autologous peripheral blood stem cell transplant in progressive hormone-refractory prostate cancer metastatic to bone. Eur J Nuc Med Mol Imaging. 2006 Sep ;33(9):1055-61. Epub 2006 Mar 30.

131. Papadimitriou C, Dafni U, Anagnostopoulos A, Vlachos G, Voulgaris Z, Rodolakis A, et al. High-dose melphalan and autologous stem cell transplantation as consolidation treatment in patients with

chemosensitive ovarian cancer: results of a single-institution randomized trial. Bone Marrow Transplant. 2007 Nov 19; [Epub ahead of print]

132. Patel MI, Motzer RJ, Sheinfeld J. Management of recurrence and follow-up strategies for patients with seminoma and selected high-risk groups. Urol Clin N Am. 2003;30:803-17.

133. Peccatori J, Barkholt L, Demirer T, Sormani MP, Bruzzi P, Ciceri F, et al. Prognostic factors for survival in patients with advanced renal cell carcinoma undergoing nonmyeloablative allogeneic stem cell transplantation. Cancer. 2005 Nov 15;104(10):2099-103.

134. Pedrazzoli P, Ledermann JA, Lotz JP, Leyvraz S, Aglietta M, Rosti G, et al. High dose chemotherapy with autologous hematopoietic stem cell support for solid tumors other than breast cancer in adults. Ann Oncol. 2006 Oct;17(10):1479-88. Epub 2006 Mar 17.

135. Peinemann F, Smith LA, Kromp M, Bartel C, Kroger N, Kulig M. Autologous hematopoietic stem cell transplantation following high-dose chemotherapy for non-rhabdomyosarcoma soft tissue sarcomas. Cochrane Database Syst Rev. 2011 Feb 16;(2): CD008216.

136. Peres E, Abidi MH, Mellon-Reppen S, Klein J, Braun T, Abella E, et al. Reduced intensity transplantation for metastatic renal cell cancer with 2-year follow-up. J Immunother. 2007 Jul-Aug;30(5):562-6.

137. Pico JL, Rosti G, Kramar A, Wandt H, Koza V, Salvioni R, et al. A randomised trial of high-dose chemotherapy in the salvage treatment of patients failing first-line platinum chemotherapy for advanced germ cell tumours. Ann Oncol. 2005 Jul;16(7):1152-9. Epub 2005 May 31.

138. Pili R, Kaufman E, Rodriquez R. Cancer of the kidney. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology.5th ed. New York, NY: Churchill Livingstone; 2013.

139. Prince HM, Rischin D, Quinn M, Allen D, Planner R, Neesham D, et al. Repetitive high-dose topotecan, carboplatin, and paclitaxel with peripheral blood progenitor cell support in previously untreated ovarian cancer: results of a phase I study. Gynecol Oncol. 2001;81:216-24.

140. Reichle A, Bolder U, Bataille F, Messmann H, Wagner H, Zaiss M, et al. A multimodal treatment approach including high-dose chemotherapy in very advanced gastric cancer: evidence for control of metastatic disease. Bone Marrow Transplant. 2003 Oct;32(7):665-71.

141. Rini BL, Halabi S, Barrier R, Margolin KA, Avagin D, Logan T, et al. Adoptive immunotherapy by allogeneic stem cell transplantation for metastatic renal cell carcinoma: a CALGB intergroup phase II study. Biol Blood Marrow Transplant. 2006 Jul;12(7):778-85.

142. Rini BI, Zimmerman T, Stadler WM, Gajewski TF, Vogelzang NJ. Allogeneic stem-cell transplantation of renal cell cancer after nonmyeloablative chemotherapy: feasibility, engraftment, and clinical results. J Clin Oncol. 2002 Apr 15;20(8):2017-24.

143. Rizzo JD, Elias AD, Stiff PJ, Lazarus HM, Zhang MJ, Oblong DJ, et al. Autologous stem cell transplantation for small cell lung cancer. Biol Blood Marrow Transplant. 2002;8(5)723-80.

144. Roigas J, Massenkeil G. Nonmyeloablative allogeneic stem cell transplantation in metastatic renal cell carcinoma: a new therapeutic option or just a clinical experiment? World J Urol. 2005 Jul;23(3):213-20. Epub 2005 Feb 1

145. Schilder RJ, Brady MF, Spriggs D, Shea T. Pilot evaluation of high-dose carboplatin and paclitaxel followed by high-dose melphalan supported by peripheral blood stem cells in previously untreated advanced ovarian cancer: a Gynecologic Oncology Group study. Gynecol Oncol. 2003;88:3-8.

146. Schilder RJ, Gallo JM, Millenson MM, Bookman MA, Weiner LM, Rogatko A, et al. Phase I trial of multiple cycles of high-dose carboplatin, paclitaxel, and topotecan with peripheral-blood stem-cell support as front-line therapy. J Clin Oncol. 2001 Feb 15;19(4):1183-94.

147. Schilder RJ, Goldberg M, Milenson MM, Movsas B, Rogatko A, Rogers B, et al. Phase II trial of induction high-dose chemotherapy followed by surgical resection and radiation therapy for patients with marginally resectable non-small cell carcinoma of the lung. Lung Cancer. 2000 Jan;27(1):37-45.

148. Schlemmer M, Wendtner CM, Falk M, Abdel-Rahman S, Lict T, Baumert J, et al. Efficacy of consolidation high-dose chemotherapy with ifosfamide, carboplatin and etoposide (HD-ICE) followed by autologous peripheral blood stem cell rescue in chemosensitive patients with metastatic soft tissue sarcomas. Oncology. 2006;71(1-2):32-9. Epub 2007 Mar 5.

149. Schmoll HJ, Kollmannsberger C, Metzner B, Hartmann JT, Schleucher N, Schoffski P, et al. Long-term results of first-line sequential high-dose etoposide, ifosfamide, and cisplatin chemotherapy plus autologous stem cell support for patients with advanced metastatic germ cell cancer: an extended phase I/II study of the German Testicular Cancer Study Group. J Clin Oncol. 2003 Nov 15;21(22):4083-91.

150. Schrader AJ, Atzpodien J. High-dose chemotherapy with autologous stem-cell transplantation in patients with pretreated advanced malignant melanoma. Ann Oncol. 2000 Oct;11(10):1361-2.

151. Secondino S, Carrabba MG, Pedrazzoli P, Castagna L, Spina F, Grosso F, et al. Reduced intensity stem cell transplantation for advanced soft tissue sarcomas in adults: a retrospective analysis of the European Group for Blood and Marrow Transplantation. Haematologica. 2007 Mar;92(3):418-20.

152. Friedlander TW, Ryan CJ, Small EJ, Torti F. Testicular cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical Oncology. 5th ed. New York: Churchill Livingstone; 2013.

153. Stiff PJ, Shpall EJ, Liu PY, Wilczynski SP, Callander NS, Scudder SA, et al. Randomized phase II trial of two high-dose chemotherapy regimens with stem cell transplantation for the treatment of advanced ovarian cancer in first remission or chemosensitive relapse: a Southwest Oncology Group study. Gynecol Oncol. 2004;94:98-106.

154. Stiff PJ, Veum-Stone J, Lazarus HM, Ayash L, Edwards JR, Keating A, et al. High-dose chemotherapy and autologous stem-cell transplantation for ovarian cancer: an Autologous Blood and Marrow Transplant Registry report. Ann Intern Med. 2000;133:504-56.

155. Takahashi Y, Harashima N, Kajjgaya S, Yokoyama H, Cherkasova E, McCoy JP, et al. Regression of human kidney cancer following allogeneic stem cell transplantation is associated with recognition of an HERV-E antigen by T cells. J Clin Invest. 2008 Mar 3;118(3):1099-1109.

156. Tamaki A, Takamatsu H, Yamazaki H, Ishiyami K, Okumura H, Ohata K, et al. Reduced-intensity unrelated cord blood transplantation for treatment of metastatic renal cell carcinoma: first evidence of cord-blood-versus-solid-tumor effect. Bone Marrow Transplant. 2006 Dec;38(11):729-32. Epub 2006 Oct 9.

157. Toh HC, Chia WK, Sun L, Thng CH, Soe Y, Phoon YP, et al. Graft-vs-tumor effect in patients with advanced nasopharyngeal cancer treated with nonmyeloablative allogeneic PBSC transplantation. Bone Marrow Transplant. 2011 Apr;46(4):573-9.

158. Ueno NT, Childs RW. What's past is prologue: lessons learned and the need for further development of allogeneic hematopoietic stem cell transplantation for renal cell carcinoma. Biol Blood Marrow Transplant. 2007 Jan;13(1):31-3.

159. Vaena DA, Abonour R, Einhorn LH. Long-term survival after high-dose salvage chemotherapy for germ cell malignancies with adverse prognostic variables. J Clin Oncol. 2003 Nov 15;21(22):4100-4.

160. Verma S, Younus J, Haynes AE, Stys-Norman D, Blackstein M, the members of the Sarcoma Disease Site Group of Cancer Care Ontario's Program in Evidence-based Care. Dose-intensive chemotherapy with growth factor or autologous bone marrow/stem cell transplant support in first-line treatment of advanced or metastatic adult soft tissue sarcoma: a clinical practice guideline. Curr Oncol. 2008 Apr;15(2):80-4.

161. Verma S, Younus J, Stys-Norman D, Haynes AE, Blackstein M, Sarcoma Disease Site Group of Cancer Care Ontario's Program in Evidence-based Care. Dose-intensive chemotherapy with growth factor or autologous bone marrow/stem cell transplant support in first-line treatment of advanced or metastatic adult soft tissue sarcoma: a systematic review. Cancer. 2008 Mar 15;112(6):1197-205.

162. Vuky J, Tickoo SK, Sheinfeld J, Bacik J, Amsterdam A, Mazumdar M, et al. Salvage chemotherapy for patients with advanced pure seminoma. J Clin Oncol. 2002 Jan 1;20(1):297-301.

163. Walker JL, Armstrong DK, Huang HQ, Fowler J, Webster K, Burger RA, et al. Intraperitoneal catheter outcomes in a phase III trial of intravenous versus intraperitoneal chemotherapy in optimal stage III ovarian and primary peritoneal cancer: a gynecologic oncology group study. Gynecol Oncol. 2006;100:27-32.

164. Yamada K, Takahashi M, Ogura M, Kagami Y, Taji H, Kamiya Y, et al. High-dose chemotherapy and autologous peripheral blood stem cell transfusion for adult and adolescent patients with small round cell sarcomas. Bone Marrow Transplant. 2007 Apr;39(8):471-6. Epub 2007 Mar 5.

165. Yun T, Lee KW, Song EG, Na II, Shin HC, Yoon SS, et al. Non-myeloablative allogeneic stem cell transplantation for metastatic renal cell carcinoma. Clin Transplant. 2007 May-Jun;21(3):337-43.

166. Zderic S. Renal and adrenal tumors in children. Urol Clin N Am. 2014;(31):607-17