SGV
SSMC

Arbeitsgruppe off-label-use

Abschlussbericht (Prüfbericht) **Datum: May 6, 2012**

1.a Wirkstoff (INN)	Bevacizumab
1.b Zugelassene Arzneimittel Handelsnamen der in der Schweiz mit diesem Wirkstoff zugelassenen Arzneimittel (ohne Berücksichtigung der Indikation) Bundesamt für Gesundheit - Spezialitätenliste	Avastin®
2. überprüfte Indikation	Advanced Epithelial Ovarian (FIGO stages III B, III C and IV) Fallopian Tube and Primary Peritoneal Cancer; for the front-line treatment.
3. Medizinische Beurteilung	
3.1 In CH für die Indikation zugelassene Arzneimittel (Alternativen)	- Cisplatin - Carboplatin - Paclitaxel - Doxorubicin - Epirubicin - Cyclophosphamid - 5-fluorouracil - Ifosfamid - Iscador
3.2. Von PDQ (Physician Data Query, NCI), ESMO, BCCA, ASCO oder anderen Guidelines erwähnte Therapien: a) Standard	**PDQ (2012):** Regimens used in first line metastatic ovarian cancer: - Cis- or Carboplatin +Paclitaxel **NCCN (2012):** - Platinum-based combination-chemotherapy **ESMO (2010):** Currently, there are no data to recommend any new two- or three-drug combination and carboplatin–paclitaxel still remains the treatment of choice.
3.2. Von PDQ (Physician Data Query, NCI), ESMO, BCCA, ASCO oder anderen Guidelines erwähnte Therapien: b) andere	**PDQ**: (March 2, 2012) „At this time, the evidence does not support use of bevacizumab as front-line therapy, because the gain in PFS comes with increased toxicity without improvement in OS or quality of life. “ **NCCN (**Guidelines Version 3.2012, MS-9**)** "The NCCN Ovarian Cancer panel had a major disagreement about recommending the addition of bevacizumab to upfront therapy with carboplatin/paclitaxel followed by maintenance Bevacizumab therapy; this disagreement is reflected in the category 3 recommendation*. A majority of panel members

	feel that bevacizumab should not be added to upfront chemotherapy in patients with ovarian cancer, because data from GOG-0218 and ICON7 have not shown a statistically significant increase in overall survival and/or quality of life." * NCCN Category 3: Based upon any level of evidence, there is major disagreement that the intervention is appropriate. **SGO** (Society of Gynaecologic Oncology) June 2011 (no update) encourages patients and providers to discuss risks, benefits and costs associated with use of bevacizumab as a component of upfront treatment and maintenance therapy.
3.3. EMA- und FDA-Status für die Indikation a) EMA	**EMA**: Approved on 22 September 2011(Full assessment report: link): Avastin, in combination with carboplatin and paclitaxel is indicated for the front-line treatment of advanced (FIGO stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer.
3.3. EMA- und FDA-Status für die Indikation b) FDA	Not submitted to the FDA Aetna insurance in the USA approved its coverage (other USA insurer see NCCN ref Avastin and the payer community) http://www.aetna.com/cpb/medical/data/600_699/0685.html
3.4. Für den Entscheid der Arbeitsgruppe relevante Studien	ICON7: Perren TJ et al.: A phase 3 trial of bevacizumab in ovarian cancer. N Engl J Med 365 (26): 2484-96, 2011. Led by the U.K. Medical Research Council Clinical Trials Unit (MRC CTU) Bevacizumab improved progression-free survival in women with ovarian cancer. According to a subset analysis, the benefits with respect to both progression-free and overall survival were greater among those at high risk for disease progression. Among the women at high risk the median overall survival was 28.8 months in the standard-therapy group and 36.6 months in the bevacizumab group, (hazard ratio for death in the bevacizumab group, 0.64; 95% CI, 0.48 to 0.85; P = 0.002). Bevacizumab was associated with more toxic effects. GOG-0218: Burger RA et al.: Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med 365 (26): 2473-83, 2011. Double blind, randomized, controlled trial that included 1,873 patients. The use of bevacizumab during and up to 10 months after carboplatin and paclitaxel chemotherapy prolongs the median progression-free survival by about 4 months in patients with advanced epithelial ovarian cancer. No overall survival advantage was seen in patients with high-risk features. There were more treatment-related deaths in the bevacizumab-throughout arm (10 of 607, 2.3%) than in the control arm (6 of 601, 1.0%).
3.5. Medizinische Beurteilung/Kommentar	Both trials showed a modest improvement in PFS when bevacizumab was added to initial chemotherapy and continued through a prolonged maintenance phase. In addition, ICON7 showed a significant improvement in overall survival for a subgroup of poor-prognosis patients.
4. Ökonomische Beurteilung und Fazit	

4.1 Medikamentenkosten pro Monat (Publikumspreis des kostengünstigsten Präparates)	Fr. 3715.70
5. Fazit 5.1 Medizinisch (rot[1]/grün[2])	Grün Nur für nicht vorbehandelte Patientinnen mit Ovarialkarzinom FIGO Stadium III und IV, bei welchen der Tumor nicht vollständig reseziert werden konnte und welche von einer im Anschluss an die Chemotherapie durchzuführenden weiteren Operation (Second look mit interval debulking) nicht potenziell profitieren.
5. Fazit 5.2 Ökonomisch (rot[3]/gelb[4]/grün[5])	Gelb
6. Bemerkungen	• Dosierung von Bevacizumab: 7,5 mg/kg alle drei Wochen. • In Kombination mit Carboplatin und Paclitaxel

[1] Nutzen nicht erwiesen
[2] Nutzen erwiesen
[3] Wirkstoffkosten > CHF 8'000.-/Monat. In der Regel keine Kostenübernahme durch den Versicherer
[4] Wirkstoffkosten CHF 1'000.- bis 8'000.-/Monat. In der Regel Kostengutsprache für Behandlung bis zum Zeitpunkt der Reevaluation durch den behandelnden Onkologen.
[5] Wirkstoffkosten < CHF 1'000.- /Monat. In der Regel Kostengutsprache ohne weitere Formalitäten.