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Prognosis of Patients With Metastatic Renal Cell Carcinoma (mRCC) With Primary Resistance to Sunitinib: Is There Any Active Treatment?

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Background: Around 20% of patients (pts) with mRCC experience rapidly progressive disease (PD) with sunitinib. Although 2nd line treatment with everolimus is currently the standard of care in this setting, there is no prospective data available in this specific subgroup.
Methods: Pts with mRCC with rapid PD (within 2 or 4 cycles) on first line sunitinib, were retrospectively collected from 17 major european institutions. Clinical data, MSKCC classification and further treatment were assessed; PFS and OS were calculated (Cox model).
Results: 144 mRCC pts with rapid PD on first line sunitinib (2 cycles, n = 89 or 4 cycles, n = 55), were identified. Median age was 59, sex ratio 111 M/ 33W. Histological subtypes were clear cell (77%) and papillary carcinomas (14%), notably 17% of tumours exhibited sarcomatoid features. Nephrectomy had been performed in 85% of pts. Most pts presented with synchroneous metastatic disease (82%), prognostic classification was good in 10%, intermediate in 62% and poor in 20% of pts. Metastatic sites were respectively: lung (70%), bone (32%), liver (26%). Median OS was 6.97 months (m) [1−33], 23/144 (16%) pts are still alive with a median follow up of 9 months after sunitinib stop.
Second line treatment was administered in 82 (57%) pts: 23 with everolimus (E), 20 with temsirolimus (T) and 33 with sorafenib (S), 2 with axitinib (A), 2 with a bevacizumab+sunitinib combination and 2 with chemotherapy.
In pts receiving 2nd line treatment, median OS from beginning of 2nd line was 122 days for mTOR inhibitors (E: 151d and T: 84d), and 194d for S. Interestingly the 2 pts receiving A presented long lasting partial response (PFS: 250 and 195 days). Clinical benefit >3 months was observed in 22 pts (27%). Univariate analysis identified following prognosis factors for OS: prior nephrectomy, Karnofsky index, MSKCC score, number of metastatic sites, number of sunitinib cycles (2 vs 4), second line treatment (yes vs no), none of them remaining in multivariate analysis.
Conclusions: Pts with rapid PD on sunitinib have a very dismal prognosis. The benefit of current second line treatments is questionable. Although retrospective, this study does not suggest that mTOR inhibition is superior to VEGF inhibition. Data from ongoing prospective trials are urgently needed. Better understanding of primary resistance to sunitinib might help to identify new pathways. Therefore this study should push physicians to refer pts to investigational new drug trials.

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Weekly Paclitaxel as Third-line Chemotherapy in Patients With Metastatic Transitional Cell Carcinoma of Urothelial Tract: Results of a Phase II Study

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Background: Few data exist about third-line chemotherapy for metastatic disease. Although administered in up-front and second-line regimens, paclitaxel was never evaluated as third-line treatment. This study assessed the activity of weekly paclitaxel in patients with advanced TCC previously-treated with two chemotherapy regimens.
Materials and Methods: From March 2007 to July 2010, 22 patients with metastatic TCC were recruited: median age was 64 years (45−71 years) with a median ECOG PS of 1. Patients received weekly paclitaxel 80 mg/m^2 dd.1, 8, 15 every 28 days until appearance of progressive disease or unacceptable toxicity.
Results: All patients were evaluable for efficacy and toxicity. No patient showed complete response. Four patients (18%) had partial response, eight patients (36%) reported stable disease for a disease control rate of 54%. The median time to progression (TTP) was 4.4 months with a median overall survival (MOS) of 7.1 months. Treatment was well tolerated: no patient developed grade 4 toxicities.
Conclusions: This is the first study which evaluated the efficacy of paclitaxel as third-line chemotherapy in metastatic TCC. Despite the poor prognosis subset of patients evaluated, weekly paclitaxel showed quite positive results in terms of efficacy with a manageable profile of toxicity: its administration could be of interest in well-selected patients.

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Self Assessment of Buccodental Toxicity − Comparison of Patients With Metastatic Renal-cell Carcinoma (RCC) Treated With Sunitinib to Patients Treated With Chemotherapy

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Background: Sunitinib is a standard of care for first-line treatment of advanced or metastatic RCC. Recently, the association of sunitinib and bisphosphonates has been described to increase osteonecrosis of the jaw (Bozas *and al,* Oncologie 2010). We measured the potential impact of Sunitinib on buccodental toxicities.
Methods: Between Oct and Dec 2010, 58 patients with metastatic RCC treated by Sunitinib (S) and 52 patients treated by chemotherapy (C) agreed to fill a self administered questionnaire assessing buccodental status included varying oral hygiene/care practices, history of bisphosphonate treatment, occurence of dental or gingival pathologies during treatment, and quality of life. T-tests and Chi-square analyses were used to compare differences between the two groups.
Results: Median age of the 110 pts analyzed was 62.5 years (28−84) with majority of male in group S (73%) and female in group C (67%). Smokers were more represented in group C (23.1%) than in group S (8.6%) ($p = 0.036$). Among 58 pts in the group S, 9 had previously received bevacizumab, and 5 Sorafenib. Among 52 pts in the group C, 13 received an adjuvant chemotherapy, 39 had metastatic chemotherapy line, and 8 combination of chemotherapy and bevacizumab. Some pts in each group received bisphosphonates: 8 in group S (13.8%) and 4 in group C (7.7%) ($p = 0.306$). Higher frequencies of dental and gingival toxicities in group S were observed: pain (53.7% *vs* 46.3%, $p = 0.007$), teeth instability (43.1% *vs* 22.5%, $p = 0.037$), gingival bleeding (62% *vs* 42.4%, $p = 0.010$) and cavities (51.6% *vs*25%, $p = 0.005$). Consequently, 62% (S) *vs* 42.3% (C) needed to change their alimentary habits ($p = 0.010$). Indeed, the pts of the group S had more frequently visited their dentist within the few months following treatment to remove pathological teeth (15 patients *vs* 4 patients, $p = 0.013$). Results were similar with or without bisphosphonate treated patients.
Conclusion: Sunitinib seems to increase buccodental toxicity as compared to chemotherapy with or without bisphosphonate association. This work emphasizes the need of an optimal dental care and follow-up for patients treated with Sunitinib.

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Pilot Investigation of Cisplatin, 5-Fluorouracil and a Taxane (TPF) in Patients (pts) With Advanced Squamous-cell Carcinoma (SCC) of the Penis − Results From a Single-Institution Series

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Background: Few sparse data indicate poor to moderate activity of systemic chemotherapy in advanced penile SCC, and no definitive acquisition is available concerning timing for integrated surgery. Pts with metastatic bilateral or pelvic nodes show an overall survival (OS) of 15% and less than 10%, respectively. We evaluated TPF in either neoadjuvant (NA), adjuvant (A) or metastatic (M) setting in a single-center pilot trial.
Methods: 3−4 courses of paclitaxel 120 mg/m^2 d1 or docetaxel 75 mg/m^2 d1 + cisplatin 75 mg/m^2 d1 + 5-FU 750 mg/m^2 96hrs continuous infusion from d1, q3wks were provided. Primary endpoint (EP) was progression-free survival (PFS). Safety profile, response rate (RR) and OS were the secondary EPs. Immunostaining for p53, p16, p63, EGFR, HER2/neu and mutational analysis of EGFR were planned on available tissue.
Results: From 7/2004 to 03/2011, 46 consecutive pts were treated, 40 of them fully evaluable for response and outcome. 8 pts underwent paclitaxel-