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A Pan-European Study of Treatment (trx) Patterns and Toxicity of Angiogenesis Inhibitors in Patients (pts) With Advanced Renal Cell Carcinoma (RCC)

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Background: Multicenter studies provide valuable information regarding trx patterns and outcomes for rare cancers. Trx modalities and toxicities of sunitinib (SU), sorafenib (SOR), and bevacizumab (BEV) for advanced RCC in clinical practices across 5 Western European countries in 2005–2010 are reported here.
Material and Methods: Medical records, not part of a disease based registry, were retrospectively reviewed for 746 RCC pts in 11 tertiary oncology centers. Pts were ⩾18 years, had diagnosis of advanced RCC, received SU (n = 532), SOR (n = 159; 1 with IFN), or BEV (n = 55; 21 with IFN or temsirolimus) as first anti-angiogenic trx. Prior trx with cytokines, chemotherapy, and radiotherapy was permitted. Data were collected on all adverse events (AEs) and trx modifications, including trx discontinuation (d/c), interruption, and dose reduction. Trx duration was estimated using Kaplan–Meier analysis.
Results: Mean age ranged from 59 (y) (BEV) to 63 y (SOR). Over 74% of pts in each group were males. 31.4% (SU), 52.2% (SOR), and 61.8% (BEV) pts were cytokine pre-treated. The 2 most common any grade AEs were SU (fatigue: 61.3%, mucositis/stomatitis: 46.4%), SOR (hand-foot syndrome [HFS]: 44.7%, diarrhea: 43.4%), and BEV (fatigue: 47.3%, pain: 18.2%). Median trx duration was 10.5 months (m) for SU, 8.1 m for SOR, and 7.7 m for BEV. Among pts with trx d/c due to AEs, common AEs associated with d/c were: SU (fatigue: 61.1%), SOR (HFS: 37.5%), and BEV (fatigue: 44.4%). For SU and SOR, trx d/c within 18 weeks for any reason was 31.9% and 23.7%, respectively, with 51.8% and 43.8% of these due to AEs. Rates of trx modifications are in Table.
Conclusions: In this large chart review study, it was found that fatigue and HFS were major contributors to trx d/c, and 87−95% of pts experienced at least 1 trx mod, more than half due to AEs for oral agents (56% SU and 53% SOR). Early trx d/c was common and often due to AEs. Newer agents with better tolerability will broaden trx options.

Trx Modifications, n (%)	SU (oral) N = 532	SOR (oral) N = 159	BEV (IV) N = 55
Trx d/c	366 (69)	137 (85)	44 (80)
Due to progressive disease[a]	181 (44)	82 (62)	14 (39)
Due to AE[a]	72 (18)	16 (12)	9 (25)
Trx interruption[a]	130 (32)	36 (27)	5 (14)
Due to AE[a]	101 (25)	32 (24)	4 (11)
Dose reduction	235 (44)	45 (28)	4 (7)
Due to AE[a]	152 (37)	41 (31)	3 (8)
⩾1 any of the above modifications	507 (95)	150 (94)	48 (87)
Due to AE[a]	228 (56)	71 (53)	14 (39)

[a]Data from one site were not available. Denominators for proportions were: 409 (SU), 133 (SOR), and 36 (BEV).

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Evolution of Overall Survival in Renal Cell Carcinoma (2000−2008) − Results From a Swedish Population-based Study

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Background: Renal cell carcinoma (RCC) treatment has evolved rapidly over the past decade and recent advances of targeted therapies have greatly improved patient prognosis. However, survival data from population studies reflecting advances in clinical practice are sparse, as are insights regarding factors influencing overall survival (OS).
Methods: This register study assessed OS in patients with RCC and metastatic RCC (mRCC) diagnosed before (2000–2005) and after (2006–2008) the introduction of targeted therapies, as well as factors influencing OS in mRCC. Three Swedish national health registers were used: the Swedish Cancer register (diagnosis and death records), the National Patient Register (records of in-/out-patient data), and the Swedish Prescribed Drug Register (records of prescribed and dispensed drugs). In total, 8,009 patients diagnosed with RCC between 2000 and 2008 were identified in the Cancer register and individual patient data were merged from the other registers. 3,243 patients (40%) developed metastasis between 2000 and 2009. Multivariate analysis was performed using a Cox proportional hazards model, including estimation of adjusted OS. The regression model included the following covariates: age, gender, geographical region, institution size, nephrectomy, period of diagnosis, and tyrosine kinase inhibitor (TKI) prescription.
Results: RCC patients diagnosed between 2006 and 2008 demonstrated an improvement in OS compared with patients diagnosed between 2000 and 2005 (median adjusted OS: not reached vs. 46.7 months, respectively [HR = 0.72, 95% CI: 0.67–0.77; P < 0.001]). A similar improvement was found in mRCC patients (median adjusted OS: 16.1 vs. 10.9 months, respectively [HR = 0.76, 95% CI: 0.69–0.83; P < 0.001]). For mRCC patients, females compared with males (HR = 0.9, 95% CI: 0.81–0.99), large compared with small institutions (HR = 0.86, 95% CI: 0.79–0.93), nephrectomy (HR = 0.32, 95% CI: 0.29–0.35), diagnosis between 2006 and 2008 (HR = 0.76, 95% CI: 0.69–0.83), and a TKI prescription (HR = 0.82, 95% CI: 0.73–0.93) were all factors significantly associated with longer OS.
Conclusion: An improved OS for both the RCC and mRCC cohorts was demonstrated for the period 2006–2008 compared with 2000–2005. This confirms a change in therapeutic and diagnostic attitudes in RCC over recent years. Although the observed survival advantage is multifactorial in origin, contribution of targeted therapies is highly probable.

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Adjuvant Treatment for Resected Renal Cell Carcinoma (RCC): Are All Strategies Equally Negative? Meta-analysis of Randomized Trials (RCTs)

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Background: Adjuvant treatment with cytokines (CK) or vaccines (VAX) or other (chemotherapy, radiotherapy) for surgically removed localized RCC did not meaningfully improve outcome according to the available evidences, regardless of treatment administered. Nevertheless, in light of the current introduction of targeted agents, the different mechanism of action of the adopted drugs may hide a differential effect on outcome. A literature-based meta-analysis was performed to explore this issue.
Methods: Event-based Relative Risk Ratios (RRs) with 95% confidence intervals (CI) were extracted and cumulated according to a random-effect model from papers or presentation. Differences in 5-year relapse-free survival (RFS, primary end-point) and 5- and 2-year overall survival (OS), and 2-year RFS were explored. Testing for heterogeneity was performed as well. In order to determine eventual differential effect according to treatment (CK versus VAX versus Other), interaction was calculated ('quantitative' interaction with diamonds on the same side of the plot, 'qualitative' when diamonds on opposite sides).
Results: Eleven trials (2,956 pts) were gathered; 9 (1,948 pts), 6 (1,639 pts) and 6 (1,209 pts) were evaluable for 5-yrs RFS, 2-yrs RFS/OS and 5-yrs OS, respectively. The patient population ranged from 47 to 918 pts. A significant interaction ('quantitative' for CK versus Other; 'qualitative' for VAX versus CK or Other) according to treatment in the main outcome was found, as shown in the table.

Outcome	Sample	HR (95% CI)	p-value	Het. (p)	Interaction (p)
5-yrs RFS	Overall	1.12 (0.98, 1.27)	0.088	0.023	**0.035**
	CK	1.12 (0.98, 1.29)	0.085	0.76	
	VAX	0.91 (0.50, 1.66)	0.78	0.04	
	Other	1.23 (0.64, 1.35)	0.53	0.05	

No significant interaction was found in 2-yrs RFS (Overall RR 1.06, 95% CI 0.93, 1.20, p = 0.35; interaction p = 0.14), 5-yrs OS (Overall RR 1.23, 95% CI 1.01, 1.50, p = 0.039; interaction p = 0.11), or 2-yrs OS (Overall RR 1.11, 95% CI 0.91, 1.34, p = 0.28; interaction p = 0.58). Heterogeneity was