885P Are adverse events (AEs) predictive of nivolumab activity? Data from the Italian expanded access program in metastatic renal cell carcinoma (mRCC)

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Background: The Italian Renal Cell Cancer Early Access Program was an expanded access program that allowed access to nivolumab, for patients (pts) with mRCC prior to regulatory approval.

Methods: Pts with mRCC previously treated with agents targeting the vascular endothelial growth factor pathway were eligible to receive nivolumab 3 mg/kg once every 2 weeks. Pts included in the analysis had received $\geq$ 1 dose of nivolumab and were monitored for adverse events (AEs) using CTCAE v.4.0. Association between sex, age, BMI, metastatic sites, number and kind of previous therapies, ECOG PS and related toxicity were evaluated with a logistic regression model that identified only age $\geq$ 65 years (Odds Ratio= 1.54 (1.00-2.38; P = 0.05).

Results: A total of 389 pts were enrolled between July 2015 and April 2016, 79% after 2 or more lines of therapy. The most common any-grade treatment-related AEs were fatigue (13%) and rash (9%). Twenty-two (5.7%) pts discontinued treatment due to AEs. There were no treatment-related deaths. Treatment-related AEs (grade 1-4) were reported in 32% of pts. Median time to appearance of AEs was 1.4 months (range 0-11.4). Grade 3–4 AEs occurred in 27 (7%) pts. Of the 22 serious AEs who induced treatment discontinuation, 11 (50%) were considered irAEs including: grade 4 hyperglicemia (n = 1), grade 3 diarrhea (n = 1), grade 3 pulmonitis (n = 1), grade 3 bronchiolitis obliterans organising pneumonia (BOOP) (n = 1), grade 3 asthenia (n = 1), grade 3 hypertension (n = 1), grade 3 skin toxicity (n = 1), grade 3 tremor (n = 1), grade 2 eyelid ptosis (n = 1), grade 2 liver toxicity (n = 1), grade 2 hypothyroidism (n = 1). AEs were generally manageable with treatment as per protocol-specific guidelines. At a median follow-up of 12 months, the median progression-free survival was 4.5 months (95% CI 3.7 - 6.2), the 12-months overall survival rate was 63%. Pts with toxicity (124 pts) had a significant (P = 0.01) longer survival (1 year OS 69%) in comparison to pts who did not experience AEs (1 year OS 59%).

Conclusions: The appearance of AEs strongly correlates with survival benefit in a real-life population of mRCC pts treated with Nivolumab.

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