Association between neutrophil-to-eosinophil ratio (NER) and efficacy outcomes in the JAVELIN Renal 101 study

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JAVELIN Renal 101

SCOPE

- **We describe the association of NER with efficacy outcomes in the avelumab + axitinib and sunitinib arms from the third interim analysis (IA3) of the phase 3 randomized JAVELIN Renal 101 trial in previously untreated patients with advanced renal cell carcinoma (aRCC)**

CONCLUSIONS

- **A low NER (< median vs ≥ median) was associated with better objective response rate [ORR], progression-free survival [PFS], and overall survival [OS]) in patients with aRCC who received first-line avelumab + axitinib**
- **A low NER was associated with improved OS in the sunitinib arm, but there were no major differences in ORR or PFS**
- **Therefore, while NER may be prognostic for patients with aRCC regardless of treatment, it is potentially predictive of improved response to avelumab + axitinib**
- **Further evaluation of NER as a biomarker for response to immunotherapy-based combinations in aRCC is warranted**

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BACKGROUND

- The phase 3 JAVELIN Renal 101 trial (NCT02684006) in previously untreated patients with aRCC demonstrated significantly improved PFS (hazard ratio [HR], 0.69; 95% CI, 0.574-0.825; p<0.0001) with avelumab + axitinib vs sunitinib[1]
  - OS data were immature (HR, 0.80; 95% CI, 0.616-1.027; p=0.0392)
  - The combination arm had a higher ORR than the sunitinib arm (52.5% vs 27.3%)
- NER has emerged as a potential prognostic biomarker in aRCC[2-3]
  - Recent data suggest that a low baseline NER may be associated with improved outcomes with immuno-oncology–based combination treatment in aRCC[2-3]
  - However, robust analyses to validate NER as a prognostic biomarker for more recently approved immune checkpoint inhibitor + tyrosine kinase inhibitor combination treatment approaches in aRCC are lacking

METHODS

- We examined baseline NER and its association with efficacy outcomes in patients in the avelumab + axitinib and the sunitinib arms of JAVELIN Renal 101 (IA3 data cutoff, April 28, 2020)
- OS and PFS per blinded independent central review (BICR) using RECIST 1.1 were summarized using the Kaplan-Meier method
- The Cox proportional hazards model was fitted to compute the HR and corresponding 95% CI
- The proportion of patients with confirmed objective response was calculated with corresponding 1-sided 95% CI using the Clopper-Pearson method
- Multivariable Cox regression analyses were also used to assess and adjust the treatment effect for relevant baseline factors of potential prognostic impact
  - A stepwise selection procedure was followed to identify explanatory variables of potential prognostic value

RESULTS

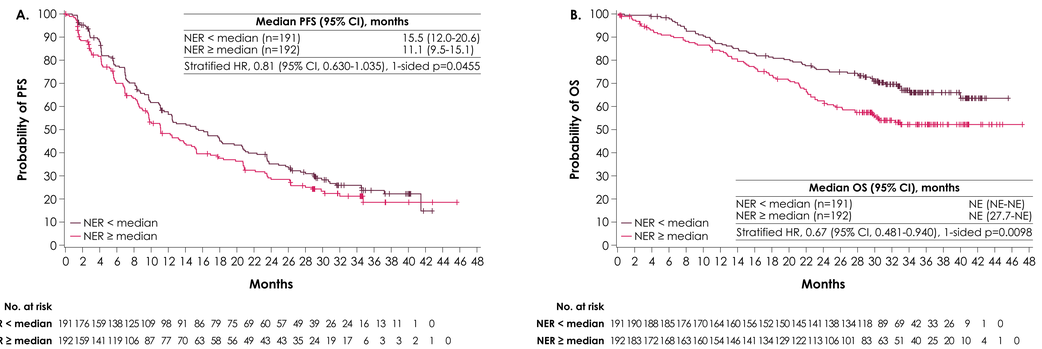
- At the cutoff date, the median NERs for the avelumab + axitinib arm (n=383) and sunitinib arm (n=396) were 29.2 and 27.0, respectively
- ORR, PFS and OS for both arms are summarized in **Table 1**
  - Better ORR (63.9% vs 55.2%) and median PFS (15.5 vs 11.1 months) were seen in patients with a NER < median vs those with a NER ≥ median, respectively, in the avelumab + axitinib arm, while no major differences in these outcomes based on NER were seen in the sunitinib arm
  - The stratified HR for PFS in patients with a NER < median compared with those with a NER ≥ median in the avelumab + axitinib arm was 0.81 (95% CI, 0.630-1.035) and 0.93 (95% CI, 0.728-1.181) in the sunitinib arm
  - Patients with a NER < median had improved OS compared with those with a NER ≥ median in the avelumab + axitinib arm (stratified HR, 0.67; 95% CI, 0.481-0.940) and the sunitinib arm (stratified HR, 0.57; 95% CI, 0.424-0.779)
- Results of the multivariate Cox regression models treating NER as a continuous variable or binary variable are consistent with the previously reported dichotomized analysis

Table 1. PFS, OS and OR by median NER

Variable	Avelumab + axitinib		Sunitinib	
	NER < median (n=191)	NER ≥ median (n=192)	NER < median (n=195)	NER ≥ median (n=201)
ORR, %	63.9	55.2	32.8	30.8
mPFS (95% CI), mo	15.5 (12.0-20.6)	11.1 (9.5-15.1)	9.7 (8.1-11.2)	8.3 (7.0-9.7)
Stratified HR (95% CI), mo 1-sided p value	0.81 (0.630-1.035) 0.0455		0.93 (0.728-1.181) 0.2700	
18-mo PFS, %	45.6	37.6	29.6	25.0
36-mo PFS, %	23.7	18.5	10.6	10.6
mOS (95% CI), mo	NE (NE-NE)	NE (27.7-NE)	NE (38.0-NE)	28.1 (22.4-35.0)
Stratified HR (95% CI), mo 1-sided p value	0.67 (0.481-0.940) 0.0098		0.57 (0.424-0.779) 0.0002	
18-mo OS, %	81.4	73.5	79.3	64.4
36-mo OS, %	66.0	52.2	62.6	41.7

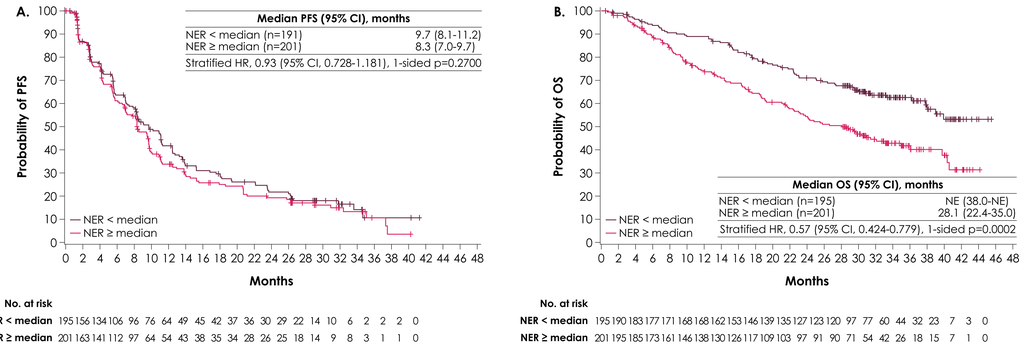
HR, hazard ratio; **mOS**, median overall survival; **mPFS** median progression-free survival; **NE**, not estimable; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival.

Figure 1. PFS per BICR and OS according to NER in the avelumab + axitinib arm



BICR, blinded independent central review; **HR**, hazard ratio; **NE**, not evaluable; **NER**, neutrophile-to-eosinophil ratio; **OS**, overall survival; **PFS**; progression-free survival.

Figure 2. PFS per BICR and OS according to NER in the sunitinib arm



BICR, blinded independent central review; **HR**, hazard ratio; **NE**, not evaluable; **NER**, neutrophile-to-eosinophil ratio; **OS**, overall survival; **PFS**; progression-free survival.

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