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Systemic Markers of Inflammation in Neuroendocrine Tumors (NETs) & Outcomes with Everolimus: A Pooled Analysis From the Randomized, Phase 3 RADIANT-3 & RADIANT-4 Trials

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BACKGROUND: The present pooled analysis evaluates the impact of systemic markers of inflammation (neutrophil-to-lymphocyte ratio [NLR] & lymphocyte-to-monocyte ratio [LMR]) at baseline on efficacy and safety among patients (pts) with NET.

METHODS: Pts with advanced, low-, or intermediate-grade pancreatic (pan), gastrointestinal (GI), or lung NETs received either everolimus (EVE) 10 mg/day oral or placebo in RADIANT-3 (pan; N=207, N=203) & RADIANT-4 (GI or lung; N=205, N=97). All pts were grouped by their median baseline values. Progression-free survival (PFS; central) was estimated by KM method & hazard ratio (HR) by unstratified Cox regression model.

RESULTS: Median PFS (95% CI) of EVE pooled population was 11.37 mo (11.01-13.93); pts with high NLR (≥ 2.5) had shorter PFS vs low NLR (< 2.5 ; 11.0 mo [8.0-12.7] vs 14.1 mo [11.2-19.2], HR 0.66, P=0.0043) & pts with low LMR (< 3.9) had

shorter PFS vs high LMR (≥ 3.9 ; 9.5 mo [7.4-11.7] vs 14.8 mo [11.2-19.4], HR 1.53, $P=0.0043$). In the overall population, pts with high NLR (≥ 2.5) had shorter PFS vs low NLR (< 2.5 ; 8.1 mo [6.3-9.2]) vs 10.8 mo [9.2-11.7], HR 0.75, $P=0.0060$) & pts with low LMR (< 3.9) had shorter PFS vs high LMR (≥ 3.9 ; 7.4 mo [5.8-8.5] vs 11.1 mo [9.3-13.7]), HR 1.46, $P<0.001$). Outcomes appeared consistent regardless of prior therapies. Whilst the above associations were observed in primary GI and panNET subgroups, they were not seen in pts with lung NET. Regarding the most common adverse events (diarrhea, stomatitis, fatigue, & rash), incidence in the NLR & LMR subgroups differed by less than 5%.

CONCLUSION: High baseline NLR & low LMR correlate with decreased PFS among pooled EVE pts, regardless of prior therapies; similar effects were noted in overall population. Safety events did not differ significantly across the high vs low subgroups of NLR & LMR.