Refining criteria of hyperprogression (HPD) with immune checkpoint inhibitors (ICIs) to improve clinical applicability

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Background: Rapid progression while on ICIs has been clinically described as HPD, however there is still not a consensus definition for this phenomenon. Institute Gustave Roussy (IGR) firstly described HPD as ≥ two-fold increase in tumor growth rate (TGR) during experimental period (EXP) vs. Reference period (REF). We recently described VHIO HPD using EXP only, as the following: PD at first restaging with ≥40% increase in sum of target lesions or ≥20% with appearance of multiple new lesions, with minimum absolute increase in measurable lesions of 10 mm (Matos I. et al. ASCO 2018).

Methods: Patients (pts) treated with ICIs in PhI trials at VHIO were analysed (n = 214). Our aim was to assess overall survival (OS) in pts who achieved PD as best response, evaluate HPD according to IGR or VHIO criteria and investigate discordance between both definitions.

Results: From Jan’12 to Oct’17, 214 pts were treated with ICIs (53% in combinations). Best response was PD in 47% pts (n = 101). Only 50 pts were evaluable for the primary endpoint (20 had PD before the first evaluation and 31 had no REF CT-scan). Using IGR criteria, median OS was 4.5 m (95% CI: 3.6-5.3) in HPD group (n = 21) versus 8.7 m (4.2-13.2) in non-HPD group (HR = 2.33; 1.10-4.95; p < 0.001). Importantly, pts with HPD by IGR had significantly lower TGR-REF (p < 0.001). Using VHIO criteria, we found no difference in TGR-REF between HPD vs non-HPD (p = 0.15). However, higher TGR-EXP was found in pts with HPD using VHIO criteria (p < 0.001).

Conclusions: We were able to validate IGR HPD criteria in our cohort, despite substantial loss in evaluable pts due to missing REF CT scans. No concordance was observed between IGR and VHIO HPD definitions. VHIO HPD criteria is strongly prognostic, easy-to-use in the clinic (EXP only) and biologically sound (not affected by small TGR during previous therapy and linked to high TGR during ICI exposure).

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