

Supplemental Table 1: Comparison of RECISTv1.1, irRC, irRECIST, imRECIST and iRECIST

	RECISTv1.1 (Eisenhauer et al., 2009)	irRC (Wolchok et al., 2009)	irRECIST (Bohnsack et al., 2013-2014)	imRECIST (Hodi et al., 2018)	iRECIST (Seymour et al., 2017)
Target Tumor	<ul style="list-style-type: none"> • 5 lesions/2 per organ max • Sum of longest diameters (SLD) • unidimensional 	<ul style="list-style-type: none"> • 10 (5 lesions per organ: 10 visceral, 5 cutaneous max) • Sum of product of two largest perpendicular diameters (SPD) • bidimensional 	<ul style="list-style-type: none"> • 5 lesions/2 per organ max • SLD • unidimensional 	<ul style="list-style-type: none"> • 5 lesions/2 per organ max • SLD • unidimensional 	<ul style="list-style-type: none"> • 5 lesions/2 per organ max • SLD • unidimensional
Non-Target lesion(s)	<ul style="list-style-type: none"> • contributes to CR/PD status 	<ul style="list-style-type: none"> • contributes to defining irCR when absent 	<ul style="list-style-type: none"> • contributes to irCR/irPD status 	<ul style="list-style-type: none"> • contributes to defining CR when absent 	<ul style="list-style-type: none"> • contributes to iCR/iUPD status
New Lesion(s)	<ul style="list-style-type: none"> • Denotes PD • Not added to tumor burden 	<ul style="list-style-type: none"> • Does not define irPD • Measurable($\geq 5 \times 5 \text{mm}$): Added to tumor burden • Non-Measurable($< 5 \times 5 \text{mm}$): precludes irCR 	<ul style="list-style-type: none"> • Does not define irPD • Measurable: Added to tumor burden • Non-Measurable: precludes irCR/contributes to irPD 	<ul style="list-style-type: none"> • Does not define PD • Measurable($\geq 5 \times 5 \text{mm}$): Added to tumor burden • Non-Measurable($< 5 \times 5 \text{mm}$): precludes CR 	<ul style="list-style-type: none"> • Denotes iUPD • Not added to tumor burden • Target new: 5 lesions/2 per organ max, obtain measurement • Non-Target new: non-measurable

Progression	<ul style="list-style-type: none"> • $\geq 20\%$ increase in SLD from nadir + 5mm absolute increase <p>and/or</p> <ul style="list-style-type: none"> • presence of new lesion <p>and/or</p> <ul style="list-style-type: none"> • unequivocal PD in non-target lesion <ul style="list-style-type: none"> • Does not require confirmation 	<ul style="list-style-type: none"> • $\geq 25\%$ increase in SPD from nadir <ul style="list-style-type: none"> • Requires confirmation >4 weeks apart 	<ul style="list-style-type: none"> • $\geq 20\%$ increase in SLD from nadir + 5mm absolute increase <p>and/or</p> <ul style="list-style-type: none"> • Unequivocal PD for non-target or new non-measurable lesions <ul style="list-style-type: none"> • Recommends confirmation >4 weeks after initial irPD assessment (particularly for those with minimal % increase above 20% threshold and during the first 12 weeks of treatment) 	<ul style="list-style-type: none"> • $\geq 20\%$ increase in SLD from nadir <ul style="list-style-type: none"> • Negated by subsequent non-PD assessment ≥ 4 weeks from the date first documented (lack of confirmation) 	<ul style="list-style-type: none"> • $\geq 20\%$ increase in SLD from nadir + 5mm absolute increase <p>and/or</p> <ul style="list-style-type: none"> • presence of new lesion <p>and/or</p> <ul style="list-style-type: none"> • unequivocal PD in non-target lesion <ul style="list-style-type: none"> • requires confirmation 4-8 weeks from original assessment, where confirmation is obtained either by additional increase (≥ 5 mm for target or measurable new lesions, any increase for non-target or an additional number of new lesions) in the original category or iUPD in another category
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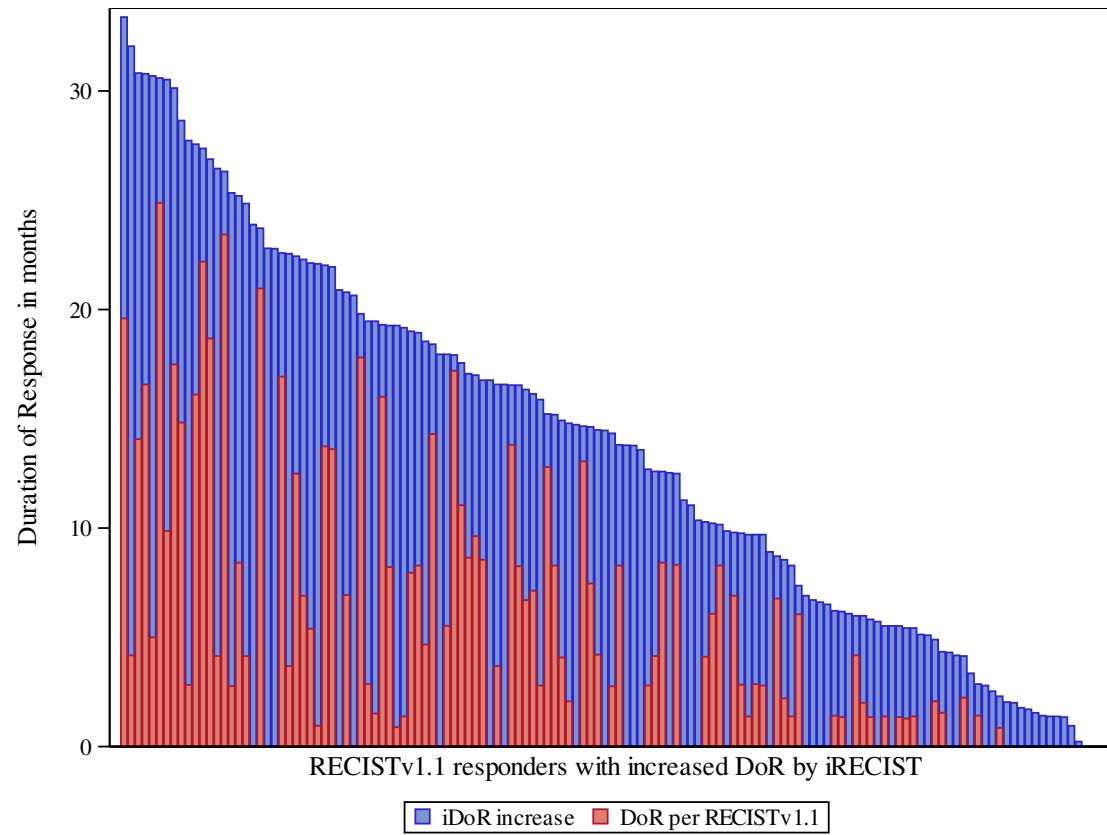
Abbreviations: SLD: Sum of longest diameter; SPD: Sum of product of two largest perpendicular diameters; PD/irPD/iUPD: progressive disease; CR/irCR: complete response

Supplemental Table 2: iRECIST and RECIST criteria for tumor response

Response Category	Criteria	FDA approach to retrospective analysis of data
iRECIST/RECIST		
iCR / CR	<ul style="list-style-type: none"> Disappearance of all non-target lesions Normalization of tumor marker level Lymph nodes <10 mm short axis 	Followed per RECISTv1.1 and iRECIST criteria
iPR / PR	≥30% decrease in target SLD, taking baseline sum as reference	Followed per RECISTv1.1 and iRECIST criteria
iSD / SD	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD	Followed per RECISTv1.1 and iRECIST criteria
iUPD / PD	<ul style="list-style-type: none"> ≥20% increase in target SLD, taking nadir sum as reference + an absolute increase ≥ 5 mm The appearance of one or more new lesions Unequivocal progression in non-target lesion 	1 st date of PD used as PFS date 1 st date of iUPD used as iPFS date if: <ul style="list-style-type: none"> It was the last assessment <u>or</u> Followed by a confirmation of PD <u>or</u> All successive assessments were iUPD
iCPD	Confirmation 4-8 weeks from original assessment with: <ul style="list-style-type: none"> Additional increase in tumor burden (i.e., ≥5 mm increase in target lesions or measurable new lesions, or any increase for non-target lesions) <u>or</u> Additional new lesions if the preceding iUPD was based on new lesions <u>or</u> iUPD in another category 	Two consecutive, non-target evaluations indicating worsening, increasing or unequivocal PD were considered confirmation, as actual measurements were not recorded to determine if there was an increase from the previous assessment
NE	For each timepoint assessment: <ul style="list-style-type: none"> If no imaging/measurement is done at all If a subset of lesion measurements is taken (and criteria for progression is not already met with the subset) 	Followed per RECISTv1.1 and iRECIST criteria

Abbreviations: iCPD: confirmed progressive disease; iCR/CR: complete response; iPR/PR: partial response; iSD/SD: Stable disease; iUPD: unconfirmed progressive disease; NE: not evaluable; PD: progression; SLD: Sum of longest diameter

Supplemental Figure 1: Duration of response by iRECIST and RECIST among n=138 responders with iSD or better post RECISTv1.1 PD.



Supplemental Figure 2: OS by (a) iPFS and (b) PFS on the log scale

