PROSTATE CANCER WORKING GROUP 3

PCWG3 – IMAGING ASSESSMENT

PCWG3 is an international working group of experts in prostate cancer who provided a framework for the assessment of subjects with castration-resistant prostate cancer enrolled in clinical trials.

KEY POINTS

Efficacy should be assessed by the interpretation of outcome measures: blood-based markers, patient reported outcomes, and imaging.

With imaging, 2 components are evaluated:

Soft tissue assessed with CT/MRI

Bone disease assessed with bone scans

Outcomes are reported by disease manifestation with radiographic progression-free survival (rPFS), defined as the time interval from enrollment to the date when the first site of disease is found to progress, or death, whichever occurs first.

SOFT TISSUE COMPONENT

ASSESSMENT ACCORDING TO RECIST 1.1 GUIDELINES.

KEY POINTS:

- Site of spread (lung, liver, adrenal, central nervous system) to be recorded separately to address disease heterogeneity.
- Bone lesions (even with soft tissue component) shouldn't be considered on CT/MRI as they will be evaluated separately on bone scans alone.

VIEW RECIST 1.1 GUIDELINES

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BONE LESION COMPONENT

NUMBER OF BONE LESIONS NEEDS TO BE COUNTED AT ALL TIME POINTS AND COMPARED TO EITHER BASELINE OR THE 1ST POST-TREATMENT SCAN.

SPECIFIC RULES TO DISTINGUISH FLARE FROM TRUE PROGRESSION

True Progression:

- Increase in activity due to tumor metabolism (actual radiological progression, new lesion).

Flare:

- Transient increase in activity due to bone remodelling as technetium bone scans are sensitive to osteoblastic activity.
- Can occur in the first 12 weeks following treatment initiation.
- Risk of discontinuing treatment prematurely if interpreted as progression.

KEY POINTS

- New lesions are considered differently if they appear within the flare period or after.
- 2+2 rule must be applied to determine progression:

  During flare period:
  2 new lesions on the 1st post-treatment scan + 2 additional new lesions on the subsequent scan with persistence of the original 2 lesions = progression.

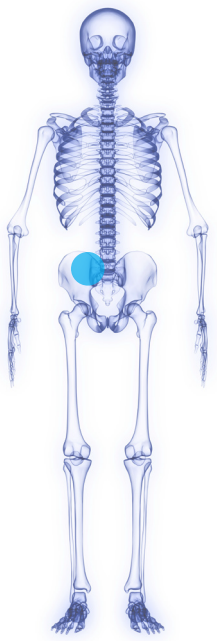
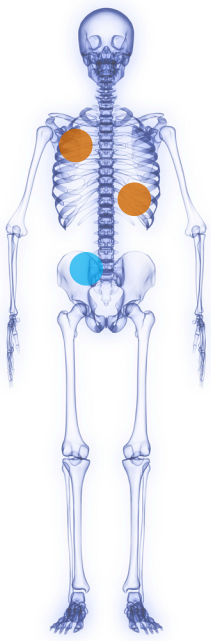
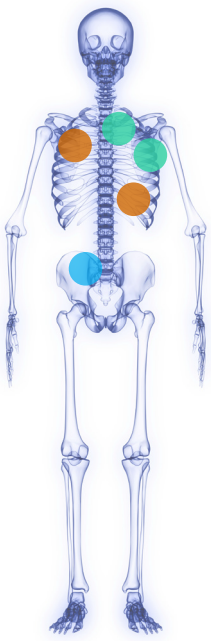
  Outside flare period:
  2 new lesions compared to 1st post-treatment scan persisting on the follow-up scan = progression.
- New lesions appearing during the flare period that are not confirmed by the 2+2 rule are regarded as flare effect and no longer contribute to overall lesion count. The first post-treatment scan becomes the new baseline against which the number of new lesions is compared.

ADDITIONAL RECOMMENDATION

The development of a superscan appearance exhibiting diffuse skeletal uptake with little or no uptake in the soft tissues calls for progression without confirmation being required.

DETERMINING PROGRESSION

Example 01

	BASELINE	FOLLOW-UP 1: 1ST POST TREATMENT SCAN	FOLLOW-UP 2
Scans			
Description	1 lesion at baseline	2 new lesions compared to baseline • Progression presumed	The 2 new lesions that appeared on the 1st post-treatment scan persist AND Presence of 2 additional new lesions • 2+2 rule met - Progression confirmed
Date of Progression	The time point that showed the first 2 lesions = Follow-up 1 (1st post-treatment scan)		

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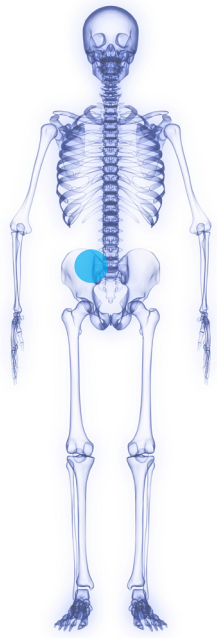
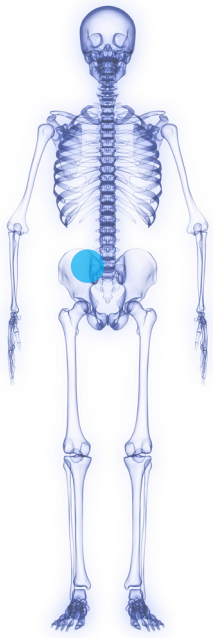
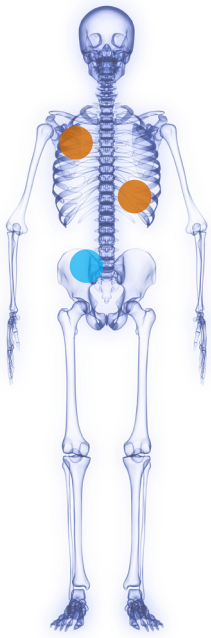
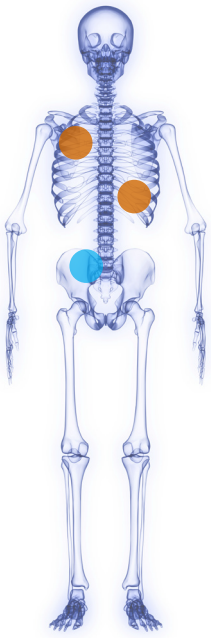
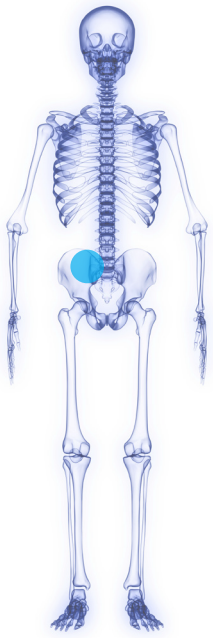
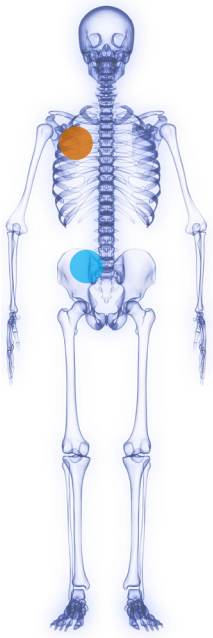
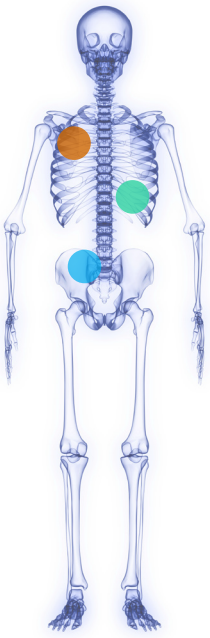
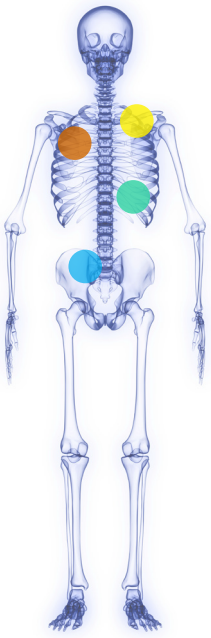
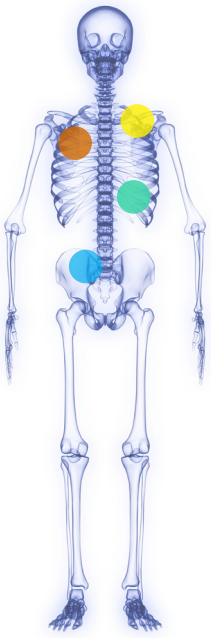
DETERMINING PROGRESSION

Example 02

	BASELINE	FOLLOW-UP 1: 1ST POST TREATMENT SCAN	FOLLOW-UP 2	FOLLOW-UP 3
Scans				
Description	1 lesion at baseline	0 new lesions compared to baseline	2 new lesions compared to the 1st post-treatment scan • Progression presumed	The 2 new lesions that appeared on the previous visit persist • Progression confirmed
Date of Progression	The time point that first documented the 2 new lesions = Follow-up 2 (2nd post-treatment scan)			

DETERMINING PROGRESSION

Example 03

	BASELINE	FOLLOW-UP 1: 1ST POST TREATMENT SCAN	FOLLOW-UP 2	FOLLOW-UP 3	FOLLOW-UP 4
Scans					
Description	1 lesion at baseline	1 new lesion compared to baseline	1 new lesion compared to the 1st post-treatment scan • 2+2 rule not met • The lesion seen on the follow-up 1 is due to flare and is no longer considered	Additional new lesion compared to the 1st post-treatment scan (2 altogether) • Progression presumed	The additional 2 new lesions (compared to the 1st post-treatment scan) persist • Progression confirmed
Date of Progression	The time point that first documents the second new lesion = Follow-up 3 (3rd post-treatment scan)				

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PCWG3 – IMAGING ASSESSMENT

KEOSYS Medical Imaging

Bone lesion assessment at Keosys

Assessment	Definition
PDu	PD is presumed because: • 2 new bone lesions have appeared within the flare window compared to baseline. OR • 2 new bone lesions have appeared outside the flare window compared to the first post-treatment scan. *Note: if there is no following visit (final visit), the time point remains at PDu.*
PD	**Only possible after PDu** PD is assigned: • If 2 new bone lesions had appeared within the flare window compared to baseline (PDu), and 2 additional new bone lesions have been found on the next scan confirming progression (PD). • The date of progression is the date of the scan showing the first 2 lesions. OR • If 2 new bone lesions had appeared outside the flare window compared to the first post-treatment scan (PDu), and the 2 lesions are persistent on the next scan confirming progression (PD). • The date of progression is the data of the scan that first documents the second lesion.
NED	No bone lesions are present on the scan (whether some were present at baseline and have completely disappeared or whether there were no bone lesions from the start).
NE	When imaging is entirely missing or was not done, but bone lesions were present at baseline.
Non-PD	Neither PD, PDu, NED or NE
Key	**PDu** = Progressive Disease Unconfirmed **PD** = Progressive Disease **NED** = No Evidence of Disease **NE** = Non-Evaluable

REFERENCE

Scher, H. I., Morris, M. J., Stadler, W. M., Higano, C., Basch, E., Fizazi, K., Antonarakis, E. S., Beer, T. M., Carducci, M. A., Chi, K. N., Corn, P. G., de Bono, J. S., Dreicer, R., George, D. J., Heath, E. I., Hussain, M., Kelly, W. K., Liu, G., Logothetis, C., Nanus, D., ... Prostate Cancer Clinical Trials Working Group 3 (2016). Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 34(12), 1402–1418. https://doi.org/10.1200/JCO.2015.64.2702