

# Radiological patterns of tumor progression in patients treated with a combination of immune checkpoint blockers and antiangiogenic drugs

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## BACKGROUND

- Immune checkpoint blockers (ICB) are widely used in oncology and steadily more in combination, especially with antiangiogenic drugs (AD)
- Usual radiological assessment is based on the change in tumor burden with “Response evaluation criteria in solid tumors” (RECIST v 1.1)
- With ICB alone or in combination, new criteria are necessary due to the risk of lesions increase or appearance of new lesions at the treatment initiation (probably in line with T-cell activation) with iRECIST and irRECIST.
- Recently, atypical responses (AR) have been described with ICB
  - Pseudoprogessions** (PsP) never exceeds 10% : apparent progression at the beginning of the treatment followed by a response
  - Dissociated response** (DR) in 7.5% : dissociated evolution between lesions

## OBJECTIVE

- Describe **radiological patterns** of the combination of ICB and AD
- Describe **survival outcomes** of each pattern

## PATIENTS AND METHODS

- Monocentric retrospective analysis of patients enrolled in phase I trials evaluating the combination of ICB and AD at the Drug Development Department (DITEP) at Gustave Roussy.
- PFS and OS analysis for each radiological responses were calculated by the Kaplan–Meier method and compared using cox and logrank models. The threshold for statistical significance was set to p<0.05.

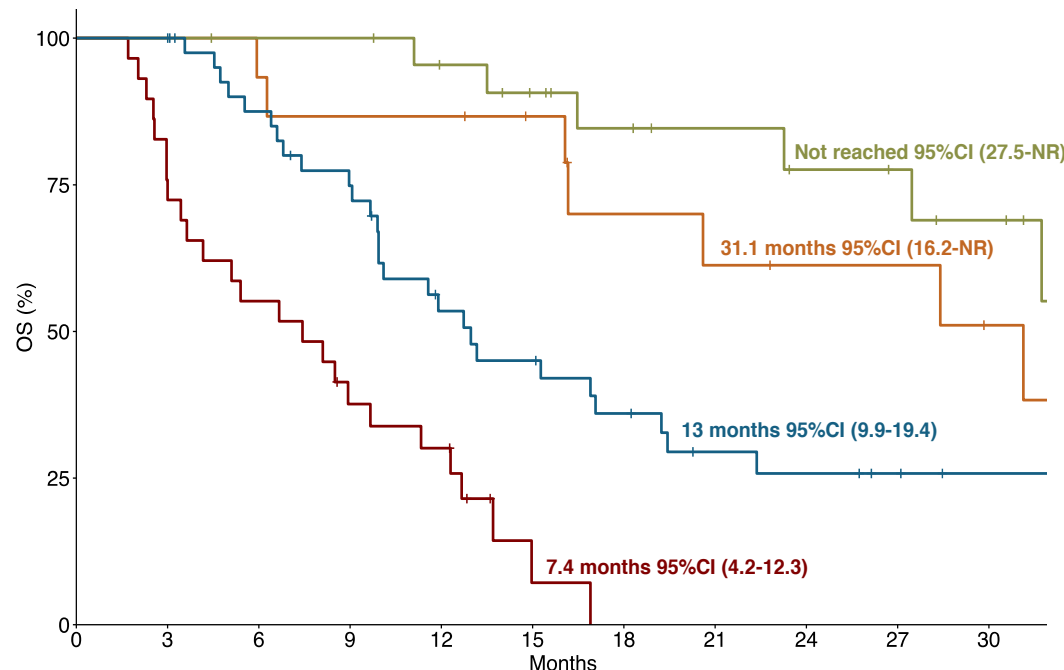
## RESULTS

	No (%)
<b>Age, median (range)</b>	63 (28-83)
<b>Gender</b>	
Male	65 (58.6%)
Female	46 (41.4%)
<b>ECOG Performans Status</b>	
0	52 (46.8%)
1	59 (53.2%)
<b>Number of Chemotherapy lines</b>	
<2	65 (58.6%)
≥2	46 (41.4%)
<b>Number of metastases sites</b>	
<2	57 (51.4%)
≥2	54 (48.6%)
<b>Type of cancer</b>	
Pleura	22 (19.8%)
Kidney	20 (18%)
Bladder	19 (17.1%)
Thymus	11 (9.9%)
Cervix	9 (8.1%)
Liver	6 (5.4%)
Ovary	6 (5.4%)
Prostate	5 (4.5%)
Oesophagus	4 (3.6%)
Others	9 (8.1%)
<b>Histology</b>	
Mesothelioma	23 (20.7%)
Squamous cell carcinoma	20 (18.0%)
Urothelial carcinoma	19 (17.1%)
Adenocarcinoma	15 (13.5%)
Clear cell carcinoma	14 (12.6%)
Hepatocellular carcinoma	6 (5.4%)
Papillary carcinoma	5 (4.5%)
Serous epithelial carcinoma	3 (2.7%)
Others	6 (5.4%)

**Table 1** : Patients characteristics (n=111)

	No (%)
<b>“Typical” responses</b>	
Response (i.e. complete or partial response)	24 (21.6)
Stable disease (SD)	43 (38.7)
Progressive disease (PD)	29 (26.1)
<b>Atypical responses</b>	
Pseudoprogession (PsP)	4 (3.6)
Dissociated response (DR)	11 (9.9)

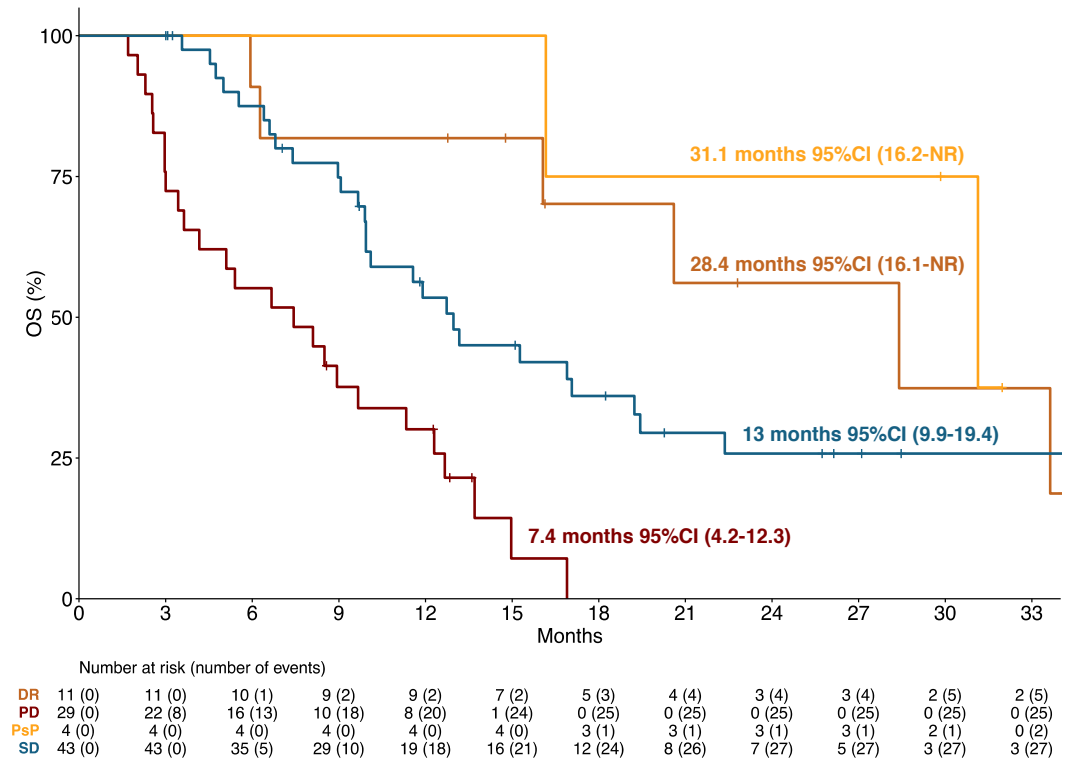
**Table 2** : Radiological patterns (n=111) with typical responses (i.e. best responses) and atypical responses in patients treated with combinaison of ICB and AD.



**Figure 1** : Overall survival (OS) according to radiological assessment between atypical responses (n=15) and typical patterns (i.e. response, SD and PD) with median (CI 95%)

	n	HR [CI 95%]	P values
<b>PD</b>	29	10.26 [3.27-32.18]	<0.0001
<b>SD</b>	43	1.99 [0.9-4.43]	0.09
<b>Response</b>	24	0.46 [0.16-1.34]	0.1

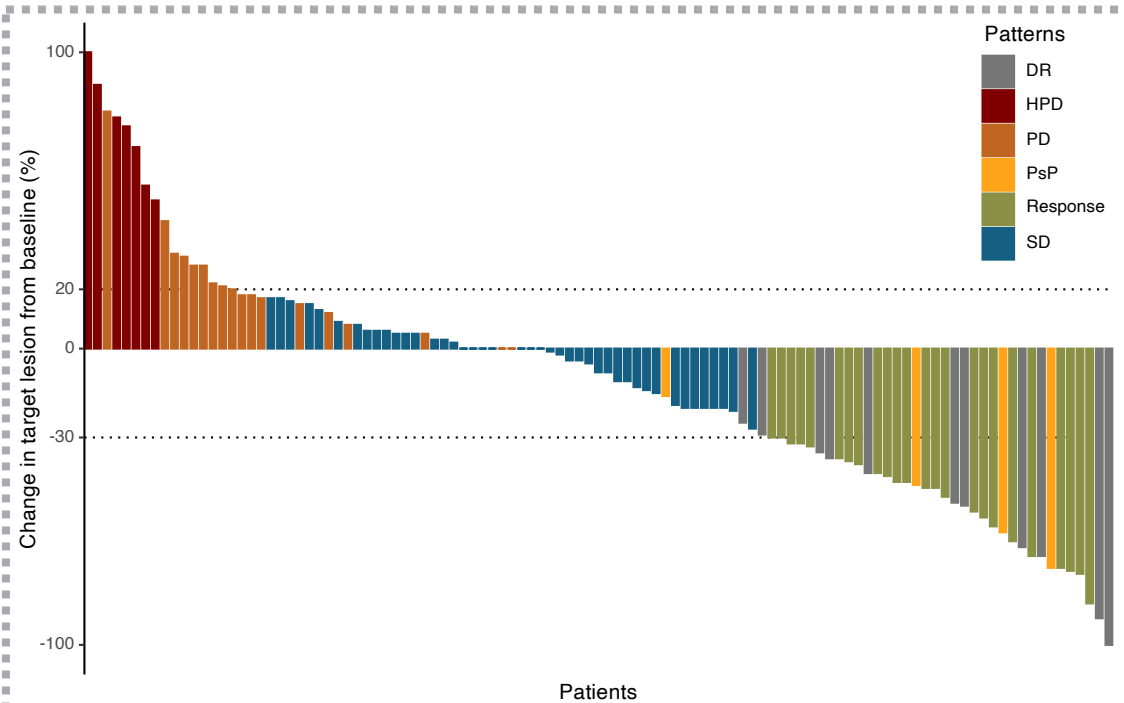
**Table 3** : Harzard ratios (log rank test) for OS comparison between each typical response vs atypical responses (n=15)



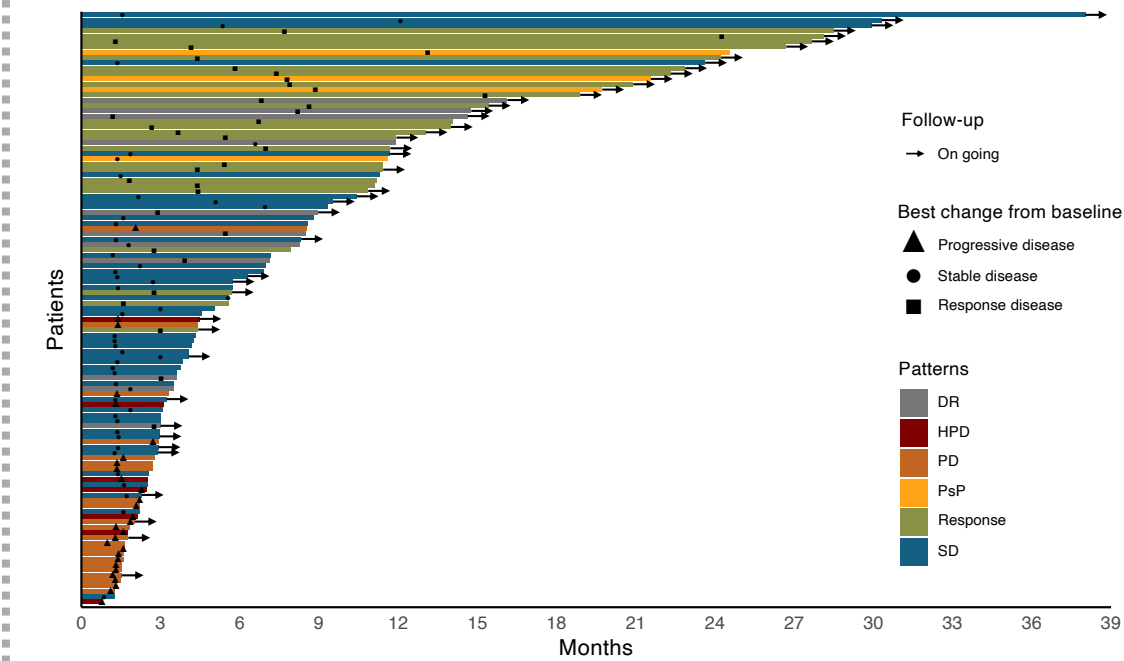
**Figure 2** : OS according to radiological assessment between PsP, DR, SD and PD with median (CI 95%).

	n	HR [CI 95%]	P values
<b>PD</b>	29	8.68 [2.45-30.76 ]	0.0001
<b>PsP</b>	4	0.61 [0.12-3.24]	0.6
<b>SD</b>	43	1.74 [0.72-4.25]	0.2

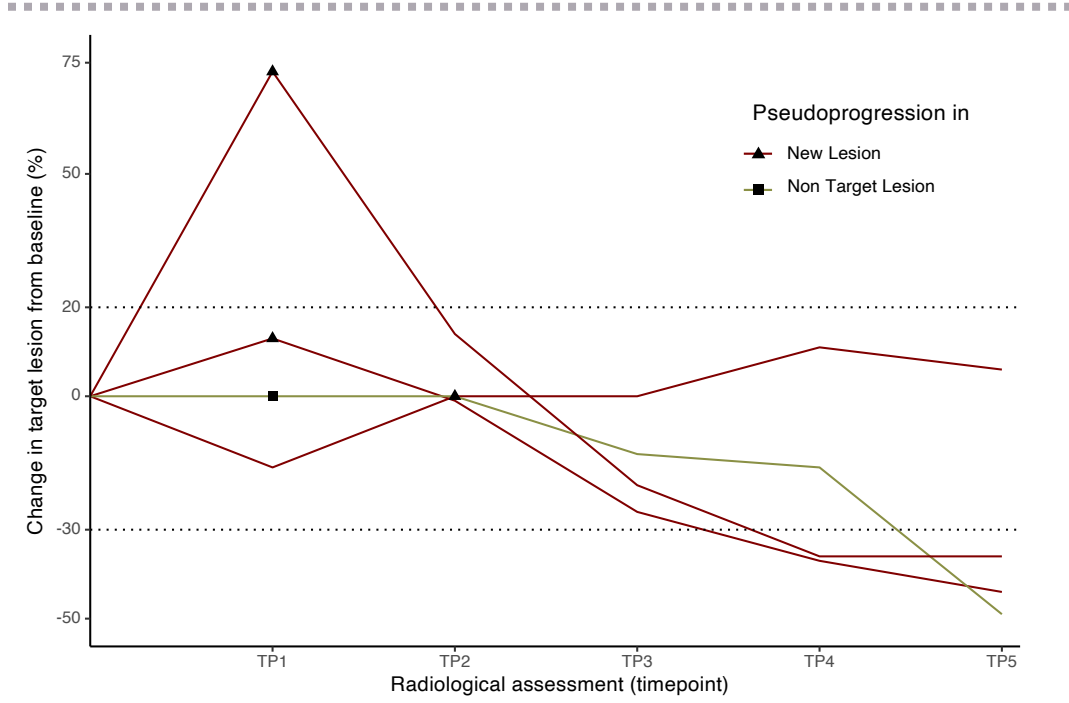
**Table 4** : Hazard ratios (log rank test) for OS comparison between PsP, SD and PD vs dissociated responses (n=11)



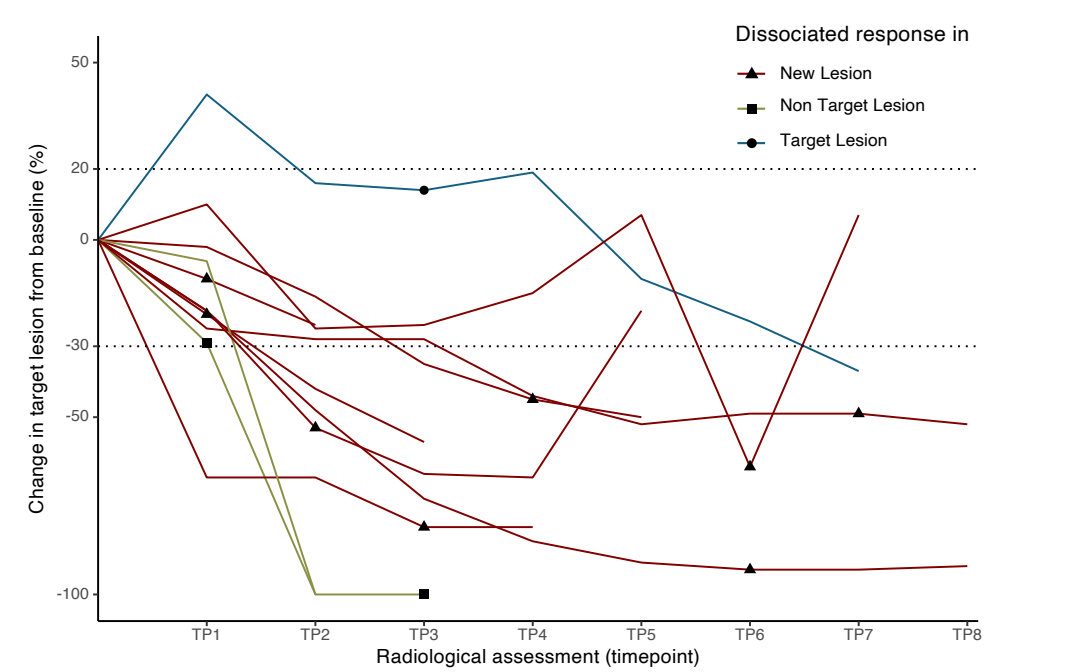
**Figure 3** : Response to combination AD and ICB : percent change in tumor burden with according to each radiological response.



**Figure 4** : Duration of response to combination of ICB and AD with best change from baseline and according to each radiological response. Arrows show patients undergoing follow-up (i.e. alive).



**Figure 5** : Spiderplot shows change in target lesion from baseline in the four patients presenting PsP. Shape indicates the lesion type and the time of PsP. (TP = time point)



**Figure 6** : Spiderplot shows change in target lesion from baseline in the eleven patients presenting DR. Shape indicates the lesion type and the time of DR. (TP = time point)

## CONCLUSION

- Patients treated with the combination of ICBs and antiangiogenic agents display atypical responses.
- Pseudoprogession and dissociated response rates were similar to previous studies. <sup>1</sup>
- Overall survival might be longer in patients with atypical response compared with progressive disease and stable disease.
- Pseudoprogession might confer a better prognosis than dissociated response.

## REFERENCES

1. E. Borcoman *et al.*, « Novel patterns of response under immunotherapy », *Ann Oncol*, vol. 30, n° 3, p. 385-396, 01 2019, doi: [10.1093/annonc/mdz003](https://doi.org/10.1093/annonc/mdz003)

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