

Supplement

Discontinuation of anti-PD-1 monotherapy in advanced melanoma - outcomes of daily clinical practice

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FIGURE S1

Figure S1 Off-treatment survival outcomes for patients who discontinued anti-PD-1 monotherapy in the absence of adverse events or progressive disease and for patients who discontinued anti-PD-1 monotherapy because of adverse events. Kaplan-Meier curves of A) overall survival and B) progression-free survival after anti-PD-1 discontinuation of patients who discontinued anti-PD-1 monotherapy in the absence of adverse events or progressive disease (log-rank $p < 0.001$ for both curves). Kaplan-Meier curves of C) overall survival and D) progression-free survival after anti-PD-1 discontinuation of patients who discontinued anti-PD-1 monotherapy because of adverse events (log-rank $p < 0.17$ and $p < 0.56$, respectively). Patient characteristics can be found in Table S1. OS - overall survival, mo - month, prob - probability, CI - confidence interval.

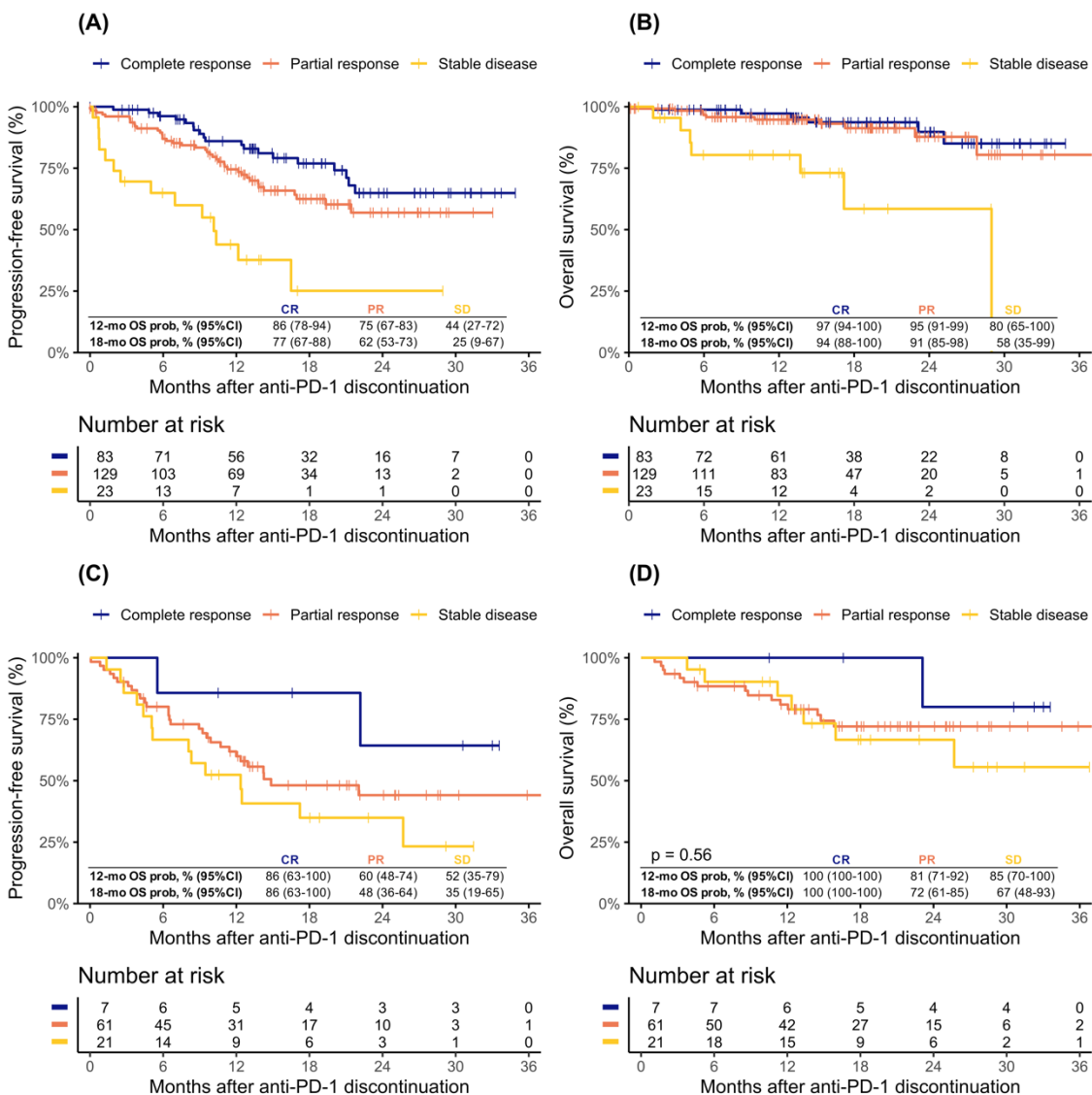


FIGURE S2

Figure S2 Second-line treatment after progression after anti-PD-1 discontinuation. For this figure re-treatment with anti-PD-1 monotherapy was considered second-line treatment.

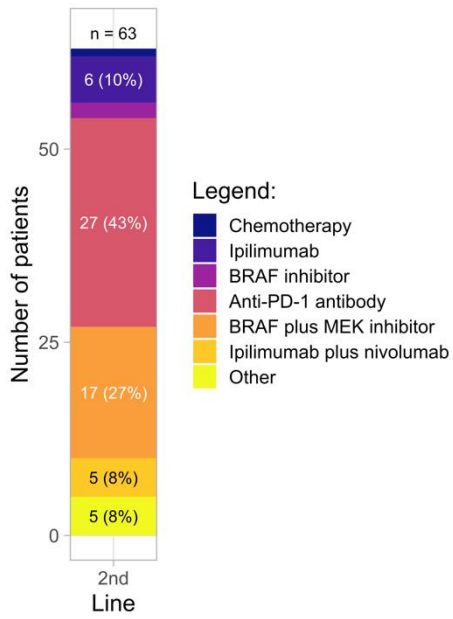
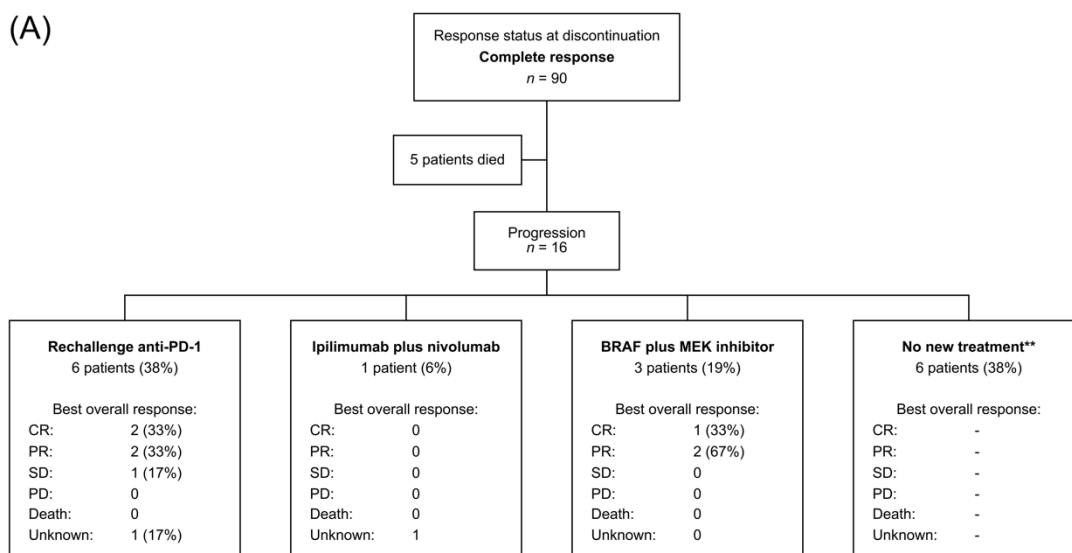


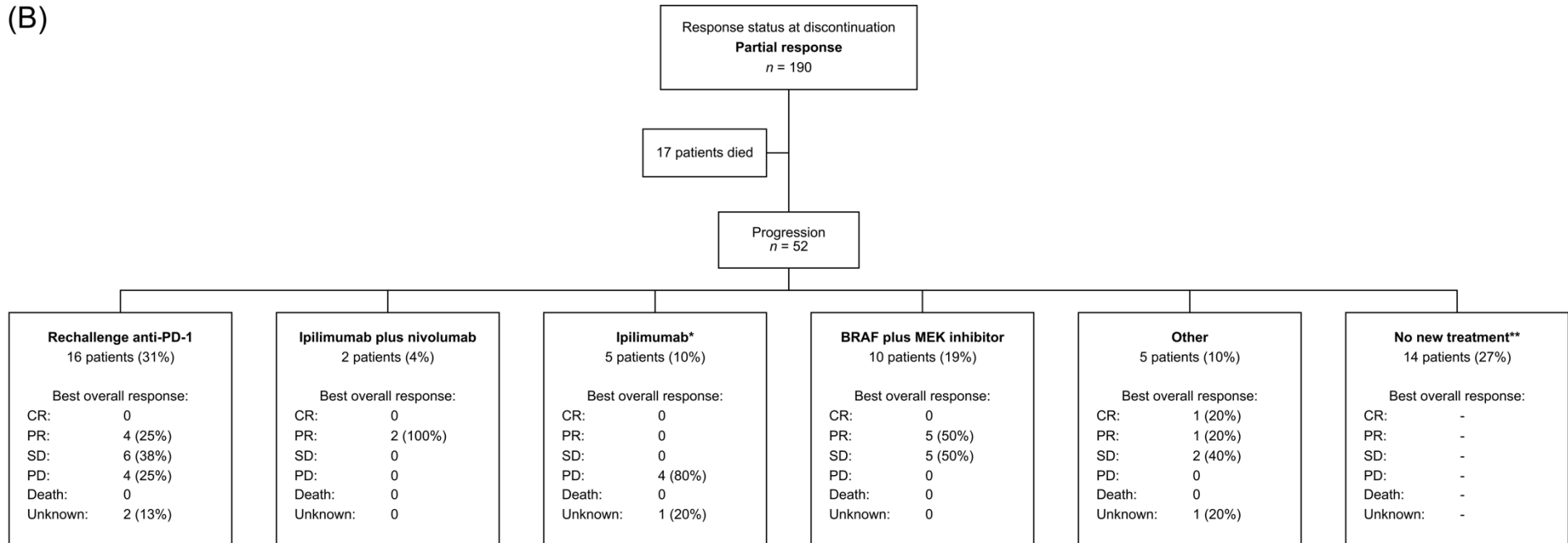
FIGURE S3

Figure S3a Best overall response of second-line treatment following progression after anti-PD-1 discontinuation for patients with a (A) complete response, (B) partial response and (C) stable disease on anti-PD-1 discontinuation. ** To date, no information on the next-line treatment received was available for these patients. CR - complete response, PR - partial response, SD - stable disease, PD - Progressive disease.

(A)



(B)



(C)

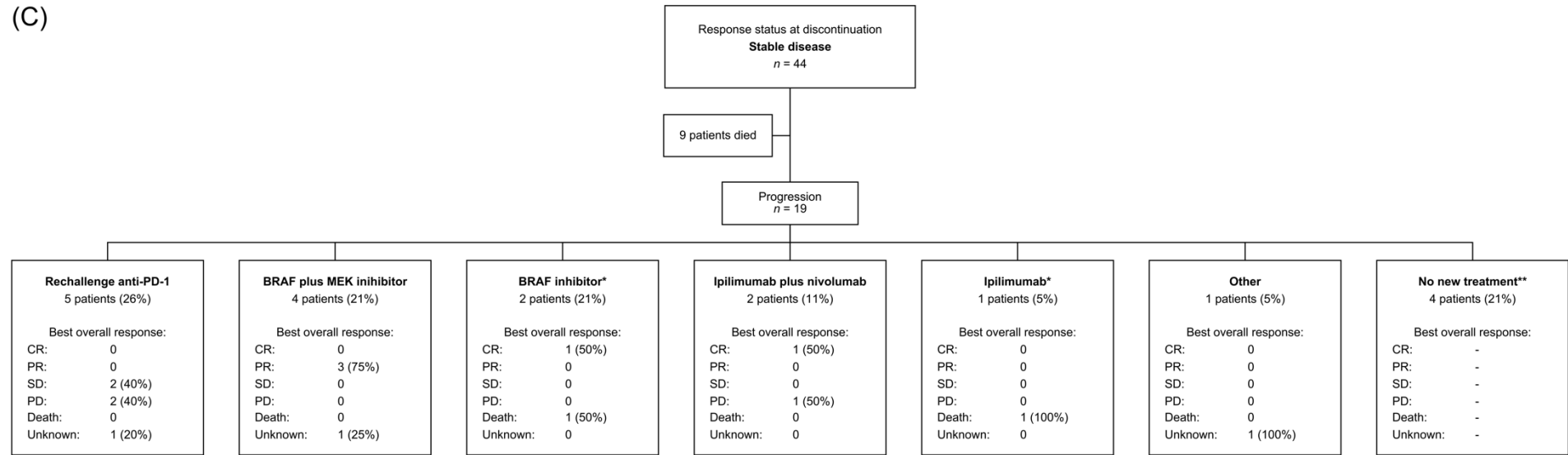


TABLE S1

Table S1 Characteristics at the start of anti-PD-1 monotherapy of patients who discontinued anti-PD-1 monotherapy in the absence of adverse events or progressive disease (elective discontinuation) and for patients who discontinued anti-PD-1 monotherapy because of adverse events (non-elective discontinuation).

| | Non-elective discontinuation (n=89) | Elective discontinuation (n=235) | P-value* |
|-------------------------------------|---|--|-----------------|
| Median age, year (IQR) | 65 [54, 72] | 71 [59, 77] | 0.004 |
| Female | 88 (37.4) | 37 (41.6) | 0.580 |
| ECOG PS | | | 0.446 |
| 0 | 156 (70.3) | 62 (71.3) | |
| 1 | 58 (26.1) | 20 (23.0) | |
| 2 | 6 (2.7) | 5 (5.7) | |
| ≥3 | 2 (0.9) | 0 (0.0) | |
| Unknown | 13 | 2 | |
| LDH level | | | 0.503 |
| Normal | 185 (79.7) | 66 (75.0) | |
| 1x ULN | 43 (18.5) | 18 (20.5) | |
| >2x ULN | 4 (1.7) | 4 (4.5) | |
| Stage | | | 0.853 |
| Unresectable IIIc | 15 (6.4) | 8 (9.0) | |
| IV-M1a | 27 (11.5) | 9 (10.1) | |
| IV-M1b | 48 (20.5) | 17 (19.1) | |
| IV-M1c | 144 (61.5) | 55 (61.8) | |
| Metastases in ≥3 organ sites | 66 (28.1) | 30 (33.7) | 0.394 |
| Liver metastasis | 40 (17.1) | 18 (20.5) | 0.592 |
| Brain metastasis | | | 0.735 |
| Absent | 199 (86.1) | 75 (84.3) | |
| Asymptomatic | 15 (6.5) | 8 (9.0) | |
| Symptomatic | 17 (7.4) | 6 (6.7) | |
| BRAF-mutant | 93 (39.6) | 34 (38.2) | 0.922 |

*P-value of statistical tests comparing characteristics of patients with a complete-, partial response and stable disease at anti-PD-1 discontinuation (excluding missing values). Categorical variables were analyzed with Chi-square test and numerical variables with the unpaired t-test. ECOG PS - Eastern Cooperative Oncology Group performance status, LDH - lactate dehydrogenase, ULN - upper limit of normal, mo - months. Values are n (%) unless otherwise indicated. Missing data of less than 2.5% is not shown.