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## **Efficacy and Safety of Anti-PD-1 Immunotherapy in Patients With Advanced NSCLC With BRAF, HER2, or MET Mutations or RET Translocation: GFPC 01-2018**

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1 **Efficacy and safety of anti-PD-1 immunotherapy in patients with advanced Non Small**  
2 **Cell Lung Cancer with *BRAF*, *HER2* or *MET* mutation or *RET*-translocation. GFPC 01-**  
3 **2018.**

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34

35

36 **Abstract**

37 **Introduction:** Immune-checkpoint inhibitor (ICI) efficacy in patients with non-small cell  
38 lung cancer (NSCLC) harboring molecular alterations remains poorly elucidated. This  
39 study was undertaken to determine ICI efficacy against *BRAF/HER2/MET/RET*-NSCLC in a  
40 real-world setting.

41 **Methods:** In this retrospective, multicenter study in ICI-treated *BRAF*-, *HER2*-, *MET*- or  
42 *RET*-NSCLCs, we analyzed clinical characteristics and outcomes: ICI-treatment duration,  
43 progression-free survival (PFS), objective response rate, duration of response (DoR), and  
44 overall survival (OS).

45 **Results:** 107 NSCLC patients (mean age, 65.5 years) were included from 21 centers: 37%  
46 never-smokers, 54% male and 93% with adenocarcinoma. Among them, 44 had *BRAF*-  
47 mutation (V600: 26), 23 *HER2* mutation, 30 *MET* mutation and 9 *RET* translocation. PDL1  
48 status was known for 45 patients:  $\geq 1\%$  in 34. Before ICI, patients had received a median  
49 of one treatment line. Median DoR, PFS and OS were 15.4 (95%CI, 12.6 – NR) months,  
50 4.7 (95%CI, 2.3–7.4) months and 16.2 (95%CI, 12.0 – 24.0) months for the entire cohort,  
51 respectively. Response rate for *BRAF*-V600, *BRAF*-nonV600, *HER2*, *MET* and *RET*-altered  
52 NSCLC was 26%, 33%, 27%, 38% and 38%, respectively. For PDL1 negative and positive  
53 patients, PFS was 3.0 (95%CI, 1.2 – NR) and 4.3 (95%CI, 2.1 – 8.5) months, respectively,  
54 and OS was 13.3 (95%CI, 4.1 – NR) and 35.2 (95%CI, 9.0 – 35.2) months, respectively.  
55 Toxicities were reported in 28 (26%) patients including 11 (10%) grade  $\geq 3$ .

56 **Conclusion:** In this real-world setting, ICI efficacy against *BRAF*-, *HER2*-, *MET*- or *RET*-  
57 NSCLC patients appeared close to that observed in unselected NSCLC patients. Large  
58 prospective studies on these patient subsets are needed.

59

60 **Keywords:** non-small-cell lung cancer; PD-1 inhibitors; *BRAF* mutations; *HER2* mutation;  
61 *MET* mutation; *RET* translocation.

62

## 63 **Introduction**

64 Management of non-small cell lung cancer (NSCLC) relies on histological subtyping  
65 and molecular analysis. In stage IV adenocarcinoma patients, *EGFR*, *ALK*, *ROS1*, *BRAF*,  
66 *MET*, *HER2* and *RET* genes are commonly assessed to offer targeted therapy for eligible  
67 patients. EGFR, ALK and ROS1 tyrosine kinase inhibitors (TKIs) are routinely used (1).  
68 Several targeted therapies have also been shown beneficial for patients with *BRAF*-,  
69 *HER2*- or *MET*-mutated and *RET*-rearranged NSCLC. Notably, treatment of BRAF-  
70 mutated NSCLC with vemurafenib, dabrafenib or the combination dabrafenib +  
71 trametinib reached over 6 and 12 months progression-free survival (PFS) and overall  
72 survival (OS), respectively(2-4). For patients with *MET* mutation, a response rate of 32%  
73 and a PFS of 7.3 months were reported with crizotinib (5). An overall response rate  
74 (ORR) of over 50% was reported with trastuzumab for HER2-mutated NSCLC (5). For  
75 RET-rearranged NSCLC, ORRs of 37%, 18%, and 22% with cabozantinib, vandetanib, and  
76 sunitinib, respectively, were reported in an international cohort study (6).

77 Besides these innovative therapeutics, immunotherapy with anti-PD1/PDL1  
78 antibodies has emerged as a standard of care in advanced NSCLC over the past 5 years.  
79 Both anti-PD-1 (nivolumab, pembrolizumab) and anti-PD-L1 (atezolizumab) immune  
80 checkpoint inhibitors (ICIs) have demonstrated their benefit in comparison with  
81 chemotherapy (7). Nevertheless, NSCLC with known oncogenic drivers have been  
82 overlooked in most studies evaluating anti-PD1/PDL1 therapy in NSCLC. As a  
83 consequence, the efficacy and safety of ICIs in these patients remains uncertain. Studies  
84 on a limited number of patients have reported mixed results in *EGFR*-, *MET*- or *HER2*-  
85 mutated and *ALK*- or *ROS1*- or *RET*-rearranged NSCLC (8-12).

86 The purpose of this retrospective study in a real-world setting was to evaluate the  
87 efficacy and safety of ICIs in *BRAF*-, *HER2*- or *MET*-mutated or *RET*-translocated  
88 advanced NSCLCs.

89

## 90 **Materials and methods**

91 *Study design and patients*

92 The IMAD2 study (GFPC 01-2018) was a retrospective, multicenter study conducted in  
93 French Lung Cancer Group (GFPC) centers. Its primary objective was to assess ICI  
94 efficacy (ORR, duration of response (DOR), PFS and overall survival (OS)) for NSCLCs  
95 harboring *BRAF*, *HER2* or *MET* mutations or *RET* translocations. The secondary objective  
96 was the assessment of safety.

97 Adult NSCLC patients were enrolled in the study when they met the following  
98 criteria: metastatic NSCLC with *BRAF*-, *HER2*- or *MET*- activating mutations or *RET*  
99 translocations; treatment with single agent anti-PD1/PDL1 ICI. Patients included in a  
100 clinical immunotherapy trial were excluded.

101

#### 102 *Molecular diagnostic*

103 Diagnostic methods used for *BRAF*, *HER2*, *MET* analysis as well as PD-L1 expression are  
104 summarized in supplementary Table S1. *RET* translocation was confirmed by Fluorescent  
105 In Situ Hybridization using Zytolight SPEC RET dual color break apart probe assay  
106 (Zytovizion, Bremerhaven, Germany) in all cases. For *BRAF* analysis, V600X mutations as  
107 well as other point mutations in exons 11 and 15 were considered. For *HER2* analysis,  
108 only exon 20 insertions were considered. For *MET* mutations, only exon 14 skipping  
109 mutations were considered.

110

#### 111 *PD-L1 expression*

112 PD-L1 expression was locally assessed by immunohistochemistry. The antibody used for  
113 staining is detailed in supplementary Table S1. Histological slides with  $\geq 100$  tumour cells  
114 were required for PD-L1 assessment. Positive PD-L1 expression was defined as PD-L1  
115 membranous staining on  $\geq 1\%$  tumour cells.

116

#### 117 *Data collection*

118 Patient demographics and clinical characteristics at NSCLC diagnosis were obtained from  
119 patient files and included: age; sex; smoker status; ethnicity; cancer stage; number and  
120 sites of metastases; presence of *BRAF*-, *HER2*- or *MET*-activating mutations, or *RET*

121 translocations; treatment lines (chemotherapy or TKIs) before ICI; the Eastern  
122 Cooperative Oncology Group performance status (ECOG PS) at immunotherapy onset;  
123 clinical response to ICI therapy; adverse event (AE) type and grade on ICI; and post-  
124 immunotherapy treatment.

125

### 126 *Statistical analyses*

127 PFS was defined as the time from ICI initiation to progression on ICI. Progression was  
128 defined as Response Evaluation Criteria In Solid Tumors version 1.1 criteria (RECIST  
129 1.1)<sup>28</sup> radiological or clinical progression (deteriorated clinical status preventing  
130 systemic treatment) or death. Assessments were done in each participating center  
131 without centralized imaging review.

132 OS was calculated from ICI introduction to death, the ORR to ICI as the best  
133 response according to RECIST1.1 (radiological assessment was done every 6 weeks). AEs  
134 were reported according to Common Terminology Criteria for Adverse Events (CTCAEs)  
135 version 4.

136 The Kaplan–Meier method was used to estimate PFS and OS for the entire cohort  
137 and according to the molecular genotypes.

138 All statistical analyses were computed with the RStudio statistical software (Version  
139 1.1.383).

140

### 141 *Ethical considerations*

142 The study was conducted in accordance with the Declaration of Helsinki. Participating  
143 centers were responsible for obtaining patient consent and institutional approval. All  
144 contributors were trained in good clinical practices. The study was purely an academic  
145 collaboration and was not funded by industry.

146

## 147 **Results**

### 148 *Patient characteristics*

149 The analysis included 107 patients managed in 21 medical centers (**Table 1**). The mean

150 ( $\pm$  standard deviation) age at diagnosis was  $65.5 \pm 10.3$  years, 57/107 (54%) patients were  
151 male and 38/107 (37%) were never-smokers. Histology was adenocarcinoma in 100/107  
152 (93%), squamous carcinoma in 3/107 (3%), large cell carcinoma in 2/107 (2%) and other  
153 in 2/107 (2%) patients. They had a median of 2 (range, 1–5) metastatic sites at diagnosis.  
154 At that time, 44/107 (41%) patients had a *BRAF* mutation (V600: 26, non-V600: 18),  
155 30/107 (34%) had a *MET* mutation, 23/107 (22%) had an *HER2* mutation, 9/107 (11%)  
156 harbored a *RET* translocation and 1/107 (1%) carried a *MET* amplification.

157 PDL1 status was known for 45/107 (42%) patients. It was negative in 11/45 (24%),  
158 positive in 34/45 (76%), including 25/45 (56%) patients with  $PDL1 \geq 50\%$ .

159 Before starting ICI therapy, patients had received a median of 1 (range, 0–5)  
160 treatment lines: ICI was the first-line treatment for 8/107 (7%), second-line treatment  
161 for 54/107 (50%), third-line treatment for 28/107 (26%), fourth-line treatment for  
162 10/107 (9%) (**Table 2**).

163

#### 164 *ICI therapy and clinical outcomes*

165 At immunotherapy initiation, ECOG PS was  $<2$  for 85/107 (80%) of the patients  
166 (**Table 1**). Immunotherapy treatments were mainly PD-1 inhibitors: nivolumab for  
167 84/107 (80%) of patients and pembrolizumab for 18/107 (17%). Twenty-one (20%)  
168 patients were treated for  $>9$  months with ICI. At data cut-off, immunotherapy was still  
169 ongoing in 16 patients, while 77 had progressed under ICI treatment. Among the 91  
170 patients who stopped immunotherapy, 39/91 (43%) patients received chemotherapy  
171 and 24/91 (26%) received a TKI post-immunotherapy. Twelve patients received local  
172 treatment for oligo-progressive disease (surgery: 2, stereotactic radiotherapy: 10) and  
173 immunotherapy was continued beyond progression in 11 patients.

174 Among 99 patients with evaluable disease, partial responses (RECIST criteria) were  
175 observed in 31 (31%) patients, stable disease in 28 (28%) and progressive disease in 39  
176 (39%) (**Table 3**). Among the 31 responders, 13 had a *BRAF* mutation, 9 had a *MET*  
177 mutation, 6 had an *HER2* mutation and 3 had a *RET* translocation. Response rates for  
178 *BRAF*-V600E, *BRAF*-nonV600E, *MET*, *HER2*, and *RET* altered NSCLC were 26%, 35%, 36%,



179 27% and 38%, respectively.

180 Median follow-up lasted 9,2 months. Median PFS for the cohort 4.7 (95% CI, 2.3–  
181 7.4) months (**Table 3, Fig. 1** and supplementary **Fig. S1**). The 6-month PFS rate was  
182 42.6% (95% CI, 33.8% - 53.7%), 12-month PFS rate was 28.0% (95% CI, 20.0% - 39.2%).  
183 Median OS for the cohort was 16.2 (95% CI, 12.0 – 24.0) months (**Table 3** and, Fig. 2 and  
184 supplementary **Fig. S2**) and 12-month OS was 58.8% (95% CI, 49.5% - 69.7%). PFS and OS  
185 according to molecular subgroup are summarized in **Table 3**.

186 The duration of response in the entire cohort was 15.4 (95%CI, 12.6 – NR) months,  
187 it was NR (95%CI, 12.6 – NR), 13.1 (95%CI, 7.6 – NR), 10.4 (95%CI, 4.6 – NR), 15.2  
188 (95%CI, 7.0 – NR) and 12.1 (95%CI, 8.4 – NR) in the *BRAF-V600-*, *BRAF-nonV600-*, *MET-*,  
189 *HER2*-mutated and *RET*-translocated patients, respectively.

190 PFS was 2.5 (95%CI, 1.5 – NR) and 4.3 (95%CI, 2.2 – 9.4) months for PDL1 negative  
191 (n=11) and positive (n=34) patients, respectively, and OS was 11.7 (95%CI, 6.8 – NR) and  
192 35.8 (95%CI, 9.3 – NR) months (**Table 4**). Efficacy results for the PD-L1 unknown and PD-  
193 L1≥50% are also presented in Table 4.

#### 194 *Safety*

195 Twenty-six (26%) patients experienced AEs, including 11 (10%) patients with grade 3–5  
196 immune-mediated AEs (5 colitis, 2 pneumonitis, 1 hypophysitis, 1 nephritis, 1 hepatitis  
197 and 1 anemia).

198

#### 199 **Discussion**

200 This retrospective study included patients with NSCLCs harboring *BRAF-*, *MET-*, and  
201 *HER2*-activating mutations, or *RET* translocations treated with ICI. Their characteristics  
202 at enrollment were as expected for a cohort of NSCLC patients with oncogenic driver  
203 mutations including a higher percentage of women and never-smokers (6, 13-19).

204 Median cohort PFS was 4.7 (95% CI, 2.3–7.4) months. Median OS was 16.2 (95% CI,  
205 12.0 – 24.0) months.

206 Four other retrospective studies have reported outcomes of *BRAF-*, *MET-* or *HER2-*  
207 mutated and *RET*-rearranged NSCLC treated with ICIs (15-19), gathering 74 *BRAF-*

208 mutated, 60 *MET*-mutated, 55 *HER2*-mutated and 16 *RET*-rearranged NSCLC patients.  
209 Our study provides a substantial number of additional cases in these rare patients,  
210 increasing each subgroup size by 40 to 60%.

211 Efficacy results for *BRAF*-mutated NSCLC are consistent between studies, with  
212 response rates of 24 to 33% reported in two previous cohorts, compared to 26 and 35%  
213 in *BRAF* V600 and non-V600 cohorts in our study (15-19). Overall, efficacy of ICI in *BRAF*-  
214 mutated NSCLC appears similar as in unselected NSCLC.

215 We found higher response rates in *HER2*- and *MET*- mutated as well as in *RET*-  
216 rearranged NSCLC patients than in previously reported studies. In all studies, tumor  
217 response was locally evaluated and might be overestimated. Better outcomes in our  
218 study might be related (i) to the high percentage of patients with PDL1 expression  $\geq 50\%$   
219 and (ii) to the relatively low number of treatments received before ICI. Of note, 9/25  
220 patients with PDL1 $\geq 50\%$  and 3/8 patients treated with ICI in the first-line setting had  
221 partial response as best response in our cohort.

222 Grade 3–5 AEs occurred in 10% of the cohort patients. Immune-mediated AEs were  
223 expected and the most frequent was colitis for 10 patients, including 5 patients with  
224 grade 3–5. These results obtained in a real-life setting confirm the good ICI safety profile  
225 reported in phase III trials.

226 Our findings do not support decreased efficacy of PD-1/PD-L1 inhibitors in patients  
227 with *MET* or *HER2* mutation or *RET* translocation. Some limitations must be taken into  
228 consideration. Response rates might be overestimated while AEs might be  
229 underestimated because of the retrospective nature of the study. PD-L1 expression  
230 could not be obtained for the majority of patients because it was not routine practice in  
231 2014-2016 in France. Nonetheless, these limitations also apply to previously reported  
232 studies. Moreover, one of our study's strengths is the enrollment of a real-life cohort  
233 composed of 107 patients with molecular alterations treated with ICI inhibitors, a rare  
234 patient profile in randomized clinical trials.

235

236 **Conclusion**

237 In this real-world setting analysis, ICI efficacy in patients with *BRAF*-, *MET*- and *HER2*-  
238 mutated or *RET*-translocated NSCLC appeared close to that observed in patients with  
239 pretreated unselected NSCLC in randomized controlled trials or observational studies.  
240 Large prospective studies are needed to determine ICI use in these rare patient subsets.

241

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245

#### 246 **Figure Legends**

247 **Figure 1.** Progression-free survival (PFS) from immunotherapy initiation for the entire  
248 cohort (A) and according to the type of molecular alteration (B).

249 **Figure 2.** Overall survival (OS) from immunotherapy initiation for the entire cohort (A)  
250 and according to the type of molecular alteration (B).

251

252 **Table 1:** Population characteristics

253 **Table 2:** Characteristics of treatment in the entire cohort and according to molecular  
254 subgroup

255 **Table 3:** Efficacy results in the entire cohort and according to molecular subgroup.

256 **Table 4:** Efficacy results according to PD-L1 status

257

258 **Supplementary Figure S1.** Kaplan-Meyer representation for Progression-Free Survival  
259 (PFS) from immunotherapy initiation for the entire cohort (A) and according to the type  
260 of molecular alteration (B).

261 **Supplementary Figure S2.** Kaplan-Meyer representation Overall Survival (OS) from  
262 immunotherapy initiation for the entire cohort (A) and according to the type of  
263 molecular alteration (B).

264

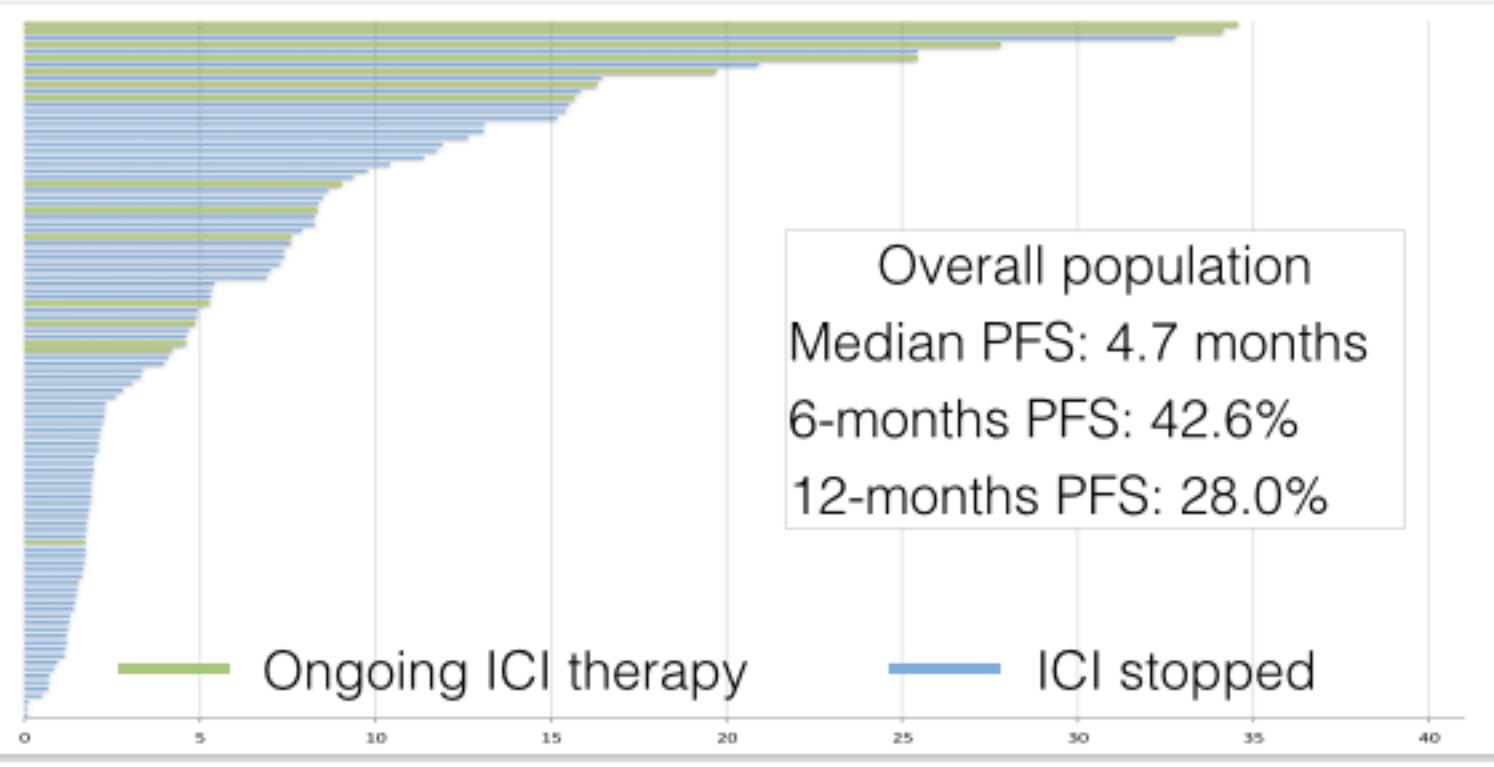
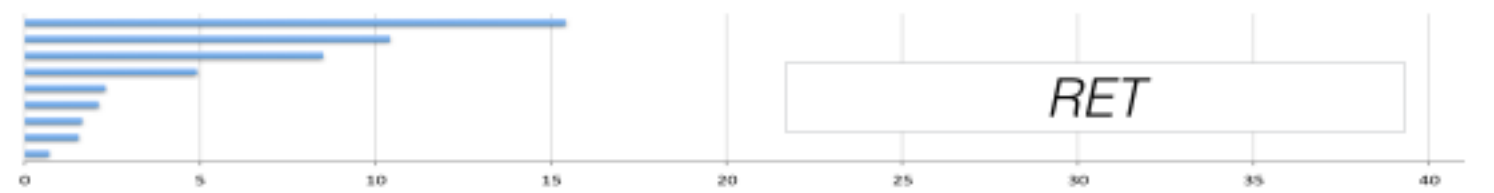
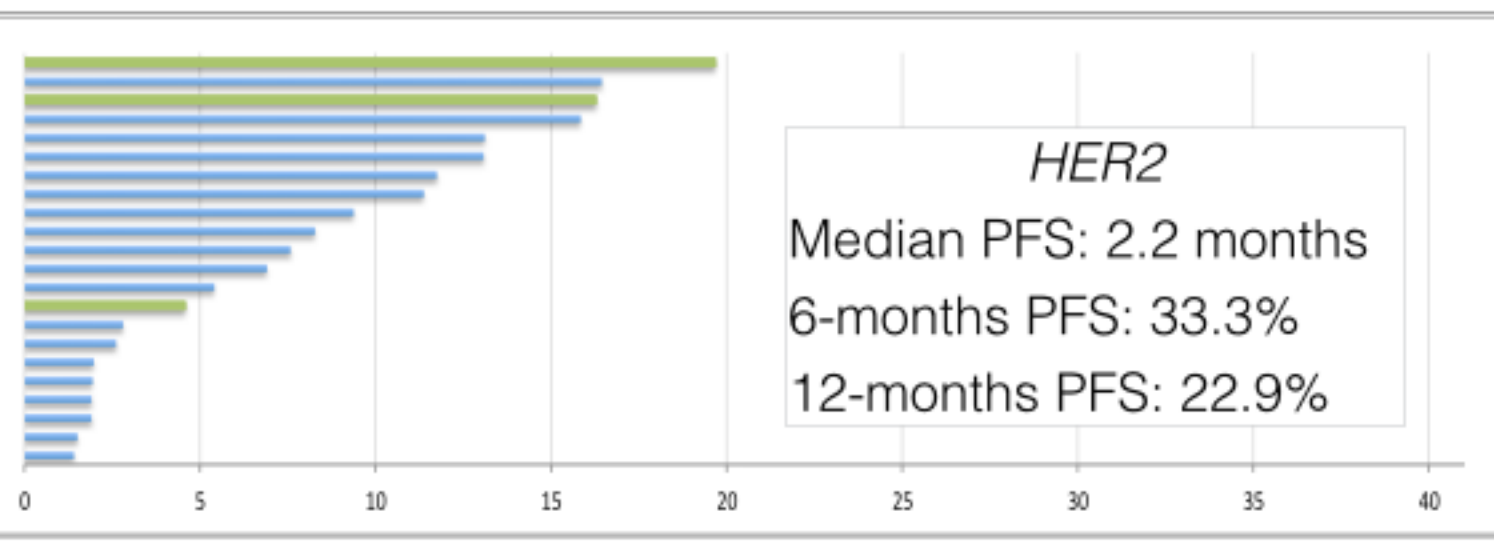
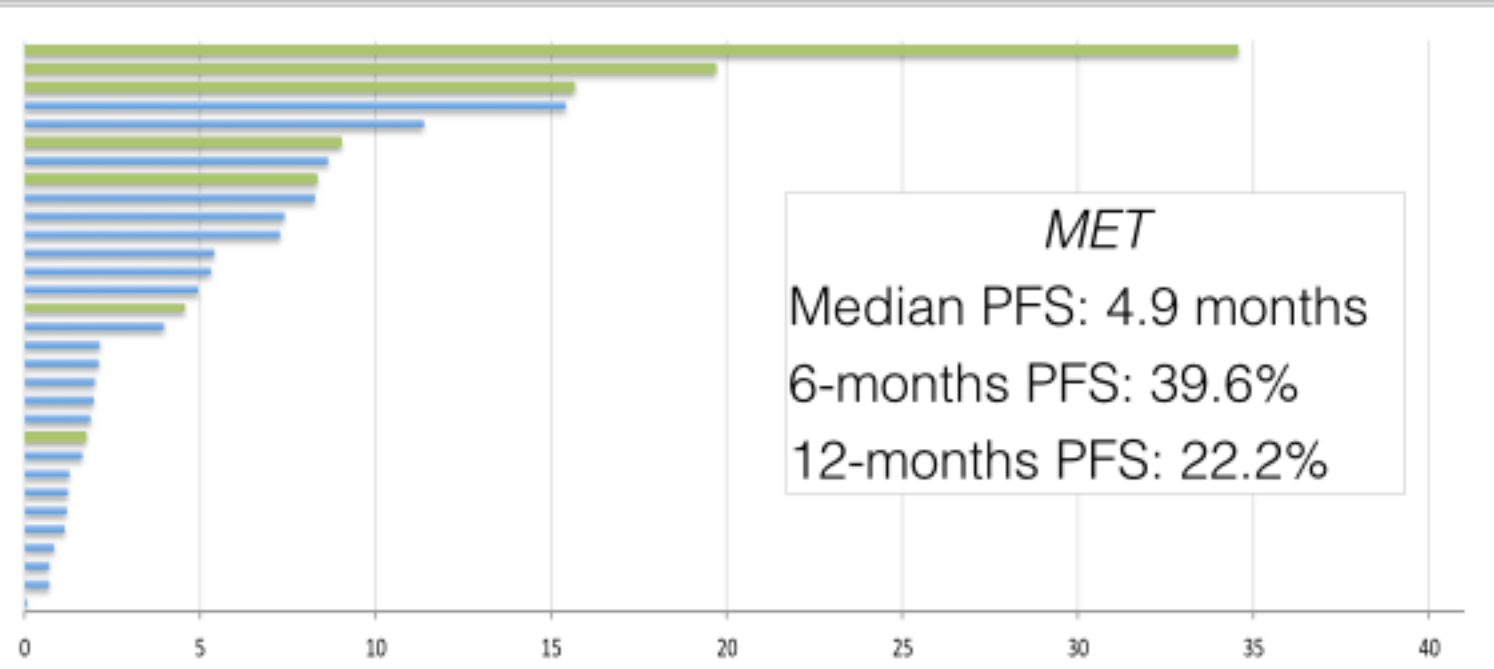
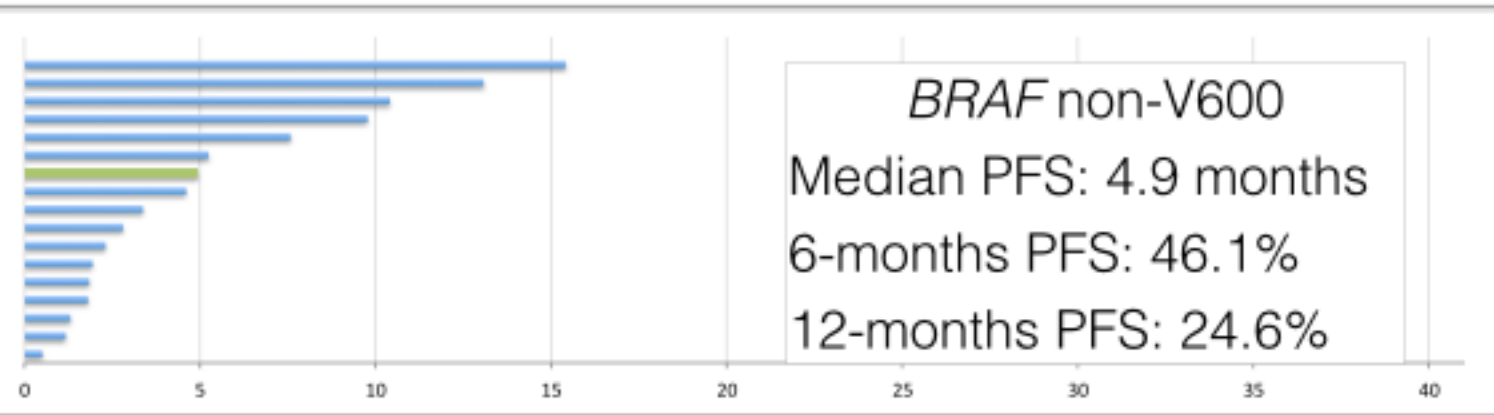
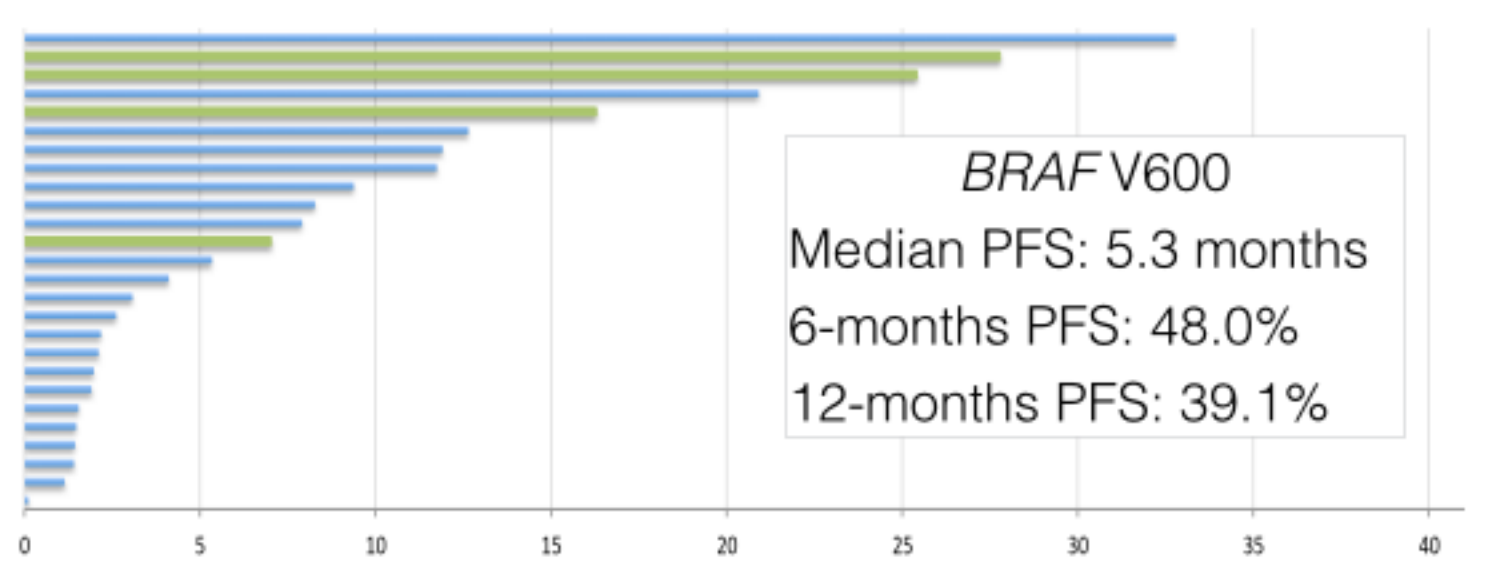
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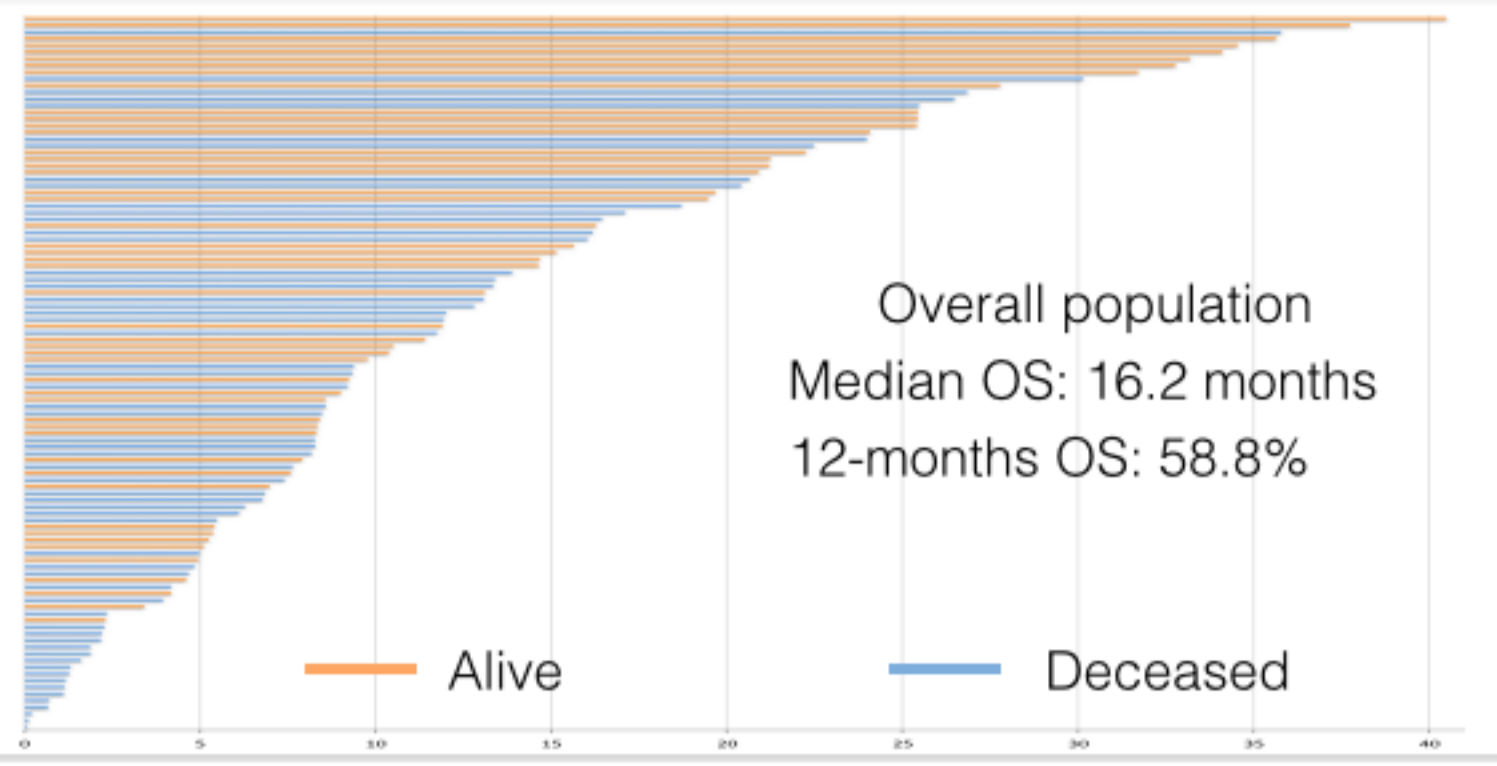
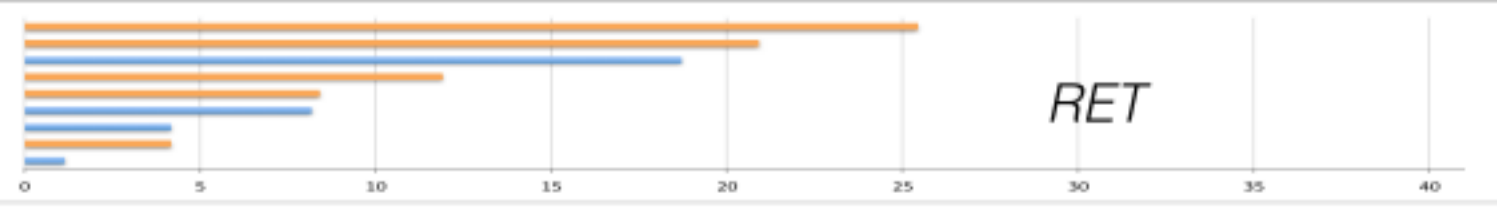
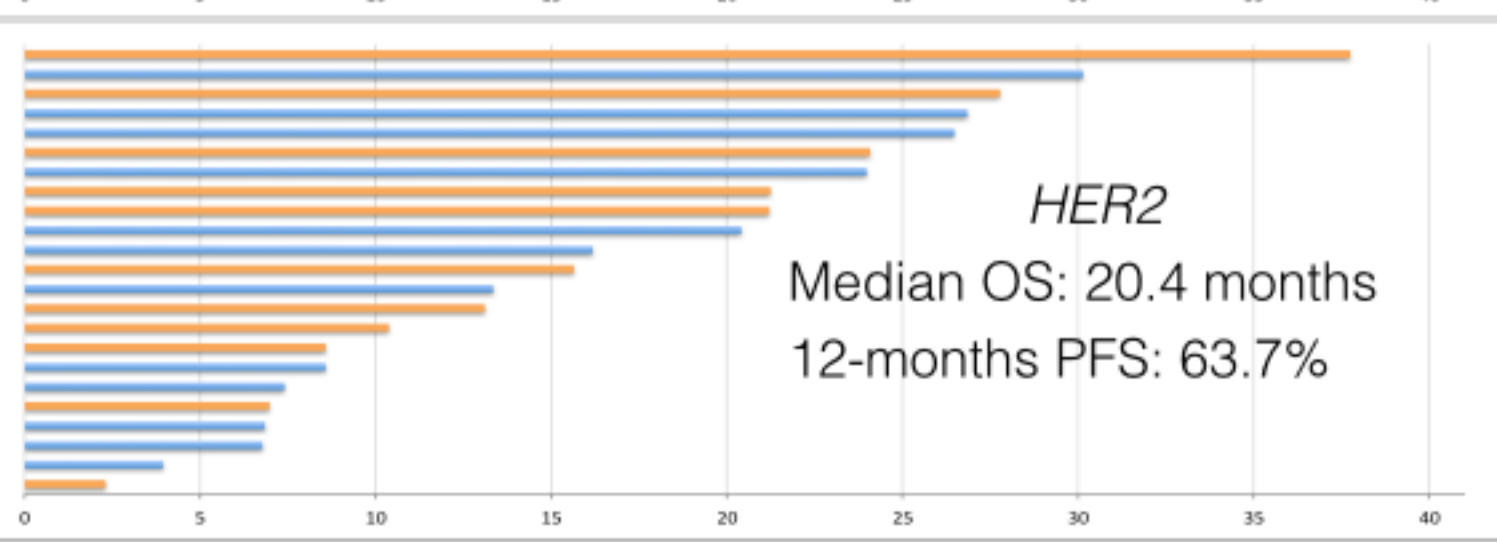
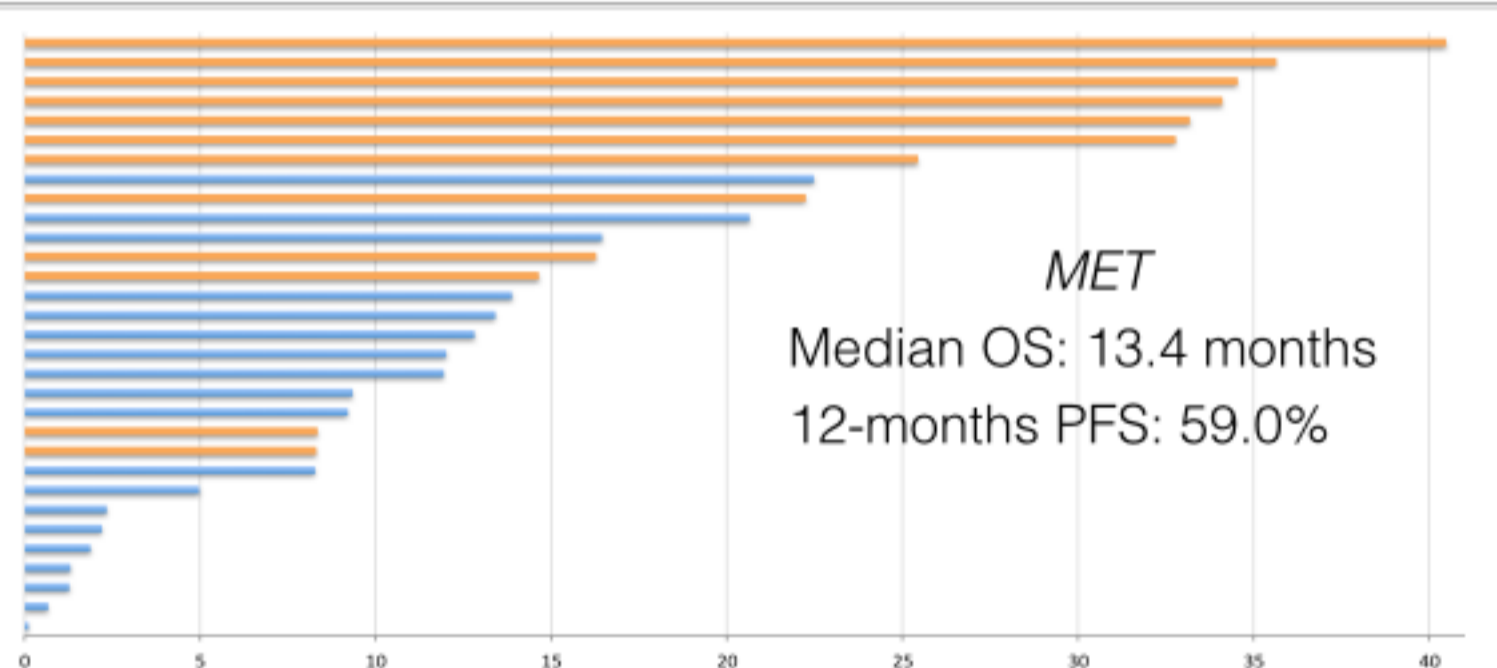
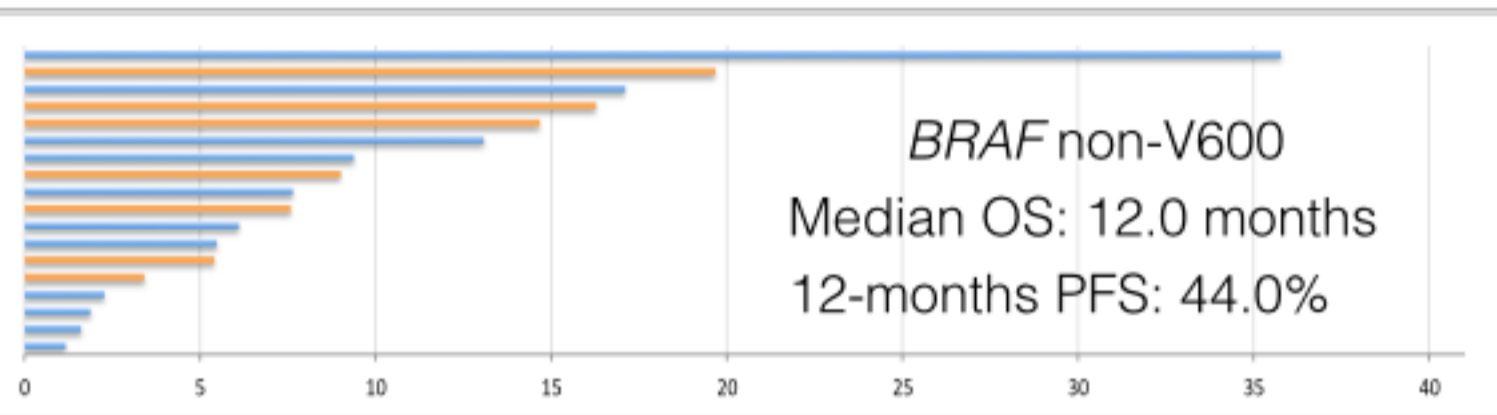
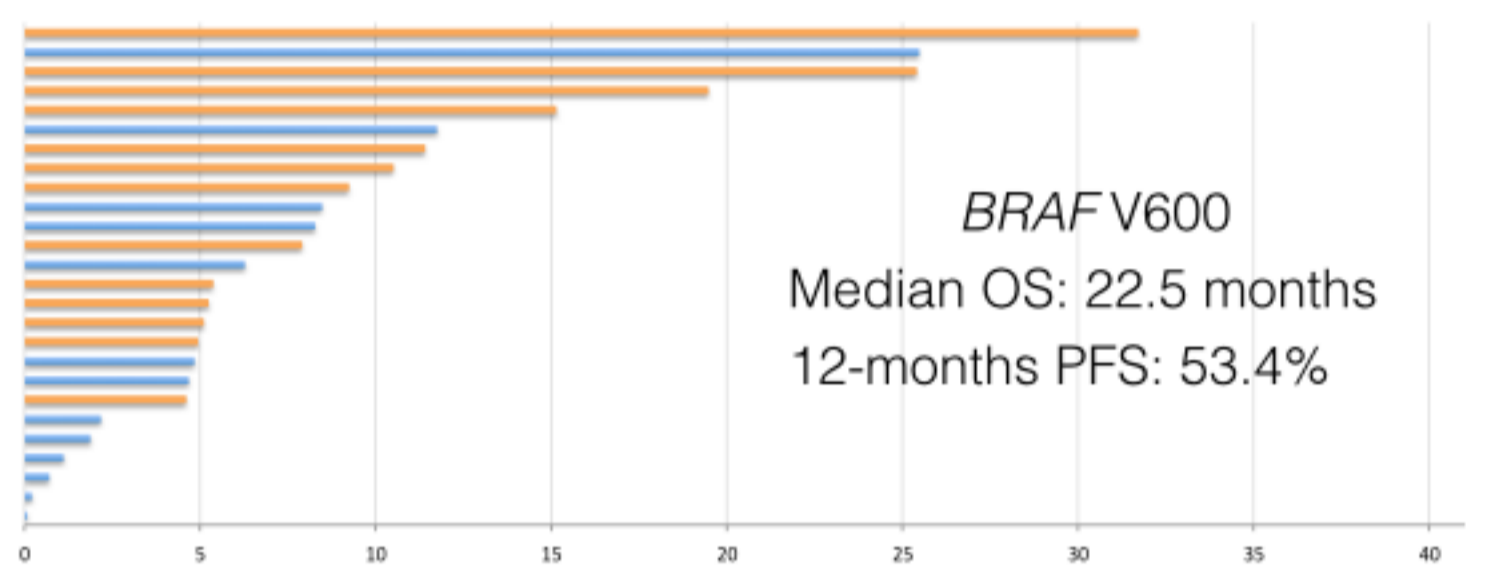
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**A****B**

**A****B**

	Total (n=107)	BRAF V600 (n=26)	BRAF nonV600 (n=18)	MET (n=30)	HER2 (n=23)	RET (n=9)
Age (mean $\pm$ SD, yr)	65.5 $\pm$ 10.3	64.9 $\pm$ 7.7	60.5 $\pm$ 12.3	64.3 $\pm$ 11.8	62.8 $\pm$ 12.7	57.8 $\pm$ 6.4
Male	57 (54%)	13 (50%)	12 (67%)	19 (63%)	8 (35%)	5 (56%)
Smoking status						
Never smoker	38 (37%)	7 (27%)	1 (6%)	11 (37%)	15 (65%)	4 (44%)
Former smoker	43 (42%)	12 (46%)	10 (56%)	11 (37%)	7 (30%)	3 (33%)
Active smoker	22 (21%)	3 (12%)	7 (39%)	8 (27%)	1 (4%)	2 (22%)
Performance status						
0-1	85 (80%)	23 (88%)	15 (83%)	22 (73%)	18 (78%)	8 (89%)
2	15 (14%)	2 (8%)	1 (6%)	7 (23%)	3 (13%)	1 (11%)
Histology						
Adenocarcinoma	100 (94%)	25 (96%)	17 (94%)	28 (93%)	22 (96%)	8 (89%)
Squamous cell carcinoma	3 (3%)	0 (0%)	0 (0%)	1 (3%)	1 (4%)	1 (11%)
Large cell carcinoma	2 (2%)	0 (0%)	1 (6%)	1 (3%)	0 (0%)	0 (0%)
Other	2 (2%)	1 (4%)	0 (0%)	1 (3%)	0 (0%)	0 (0%)
Metastatic sites						
Number (median, range)	2 (1-5)	2 (1-5)	2 (1-3)	1 (1-4)	2 (1-4)	1 (1-3)
Bone	32 (30%)	11 (42%)	5 (28%)	6 (20%)	8 (35%)	2 (22%)
Lung	25 (23%)	7 (27%)	5 (28%)	4 (13%)	8 (35%)	1 (11%)
Brain	25 (23%)	7 (27%)	2 (11%)	6 (20%)	8 (35%)	1 (11%)
Pleura	18 (17%)	5 (19%)	3 (17%)	3 (10%)	5 (22%)	2 (22%)
Lymph nodes	15 (14%)	6 (23%)	1 (6%)	1 (3%)	5 (22%)	2 (22%)
Adrenal glands	12 (11%)	3 (12%)	2 (11%)	5 (17%)	2 (9%)	0 (0%)
Liver	8 (7%)	3 (12%)	0 (0%)	1 (3%)	3 (13%)	1 (11%)
PDL1 status						
Positive	34 (32%)	11 (42%)	5 (28%)	13 (43%)	4 (17%)	3 (33%)
>50%	25 (24%)	10 (38%)	2 (11%)	11 (37%)	1 (4%)	2 (22%)
Negative	11 (10%)	3 (12%)	2 (11%)	1 (3%)	4 (17%)	5 (56%)
Unknown	62 (58%)	11 (42%)	10 (56%)	16 (53%)	15 (65%)	1 (11%)

**Table 1:** Population characteristics



	Total (n=107)	BRAF V600 (n=26)	BRAF nonV600 (n=18)	MET (n=30)	HER2 (n=23)	RET (n=9)
Line of ICI treatment						
first line	8 (7%)	3 (12%)	1 (6%)	4 (13%)	0 (0%)	0 (0%)
second line	54 (51%)	11 (42%)	11 (61%)	15 (50%)	11 (48%)	6 (26%)
third line	28 (26%)	5 (19%)	3 (17%)	6 (20%)	11 (48%)	2 (9%)
fourth line	10 (9%)	3 (12%)	3 (17%)	4 (13%)	1 (4%)	0 (0%)
> fourth line	7 (6%)	3 (12%)	0 (0%)	1 (3%)	0 (0%)	1 (4%)
Immunotherapy						
Nivolumab	84 (80%)	18 (69%)	16 (89%)	24 (80%)	19 (83%)	7 (30%)
Pembrolizumab	18 (17%)	6 (23%)	2 (11%)	6 (20%)	2 (9%)	2 (9%)
Other	4 (3%)	2 (8%)	0 (0%)	0 (0%)	1 (4%)	0 (0%)
Post immunotherapy treatment						
Chemotherapy	39					
Targeted therapy	24					
Radiotherapy	10					
Surgery	2					
Immunotherapy still ongoing	16 (15%)					

**Table 2:** Characteristics of treatment in the entire cohort and according to molecular subgroup

	Total (n=107)	BRAF V600 (n=26)	BRAF nonV600 (n=18)	MET (n=30)	HER2 (n=23)	RET (n=9)
Best response to immunotherapy						
Partial response	31 (31.3%)	6 (26.1%)	6 (35.3%)	10 (35.7%)	6 (27.3%)	3 (37.5%)
Stable disease	28 (28.3%)	8 (34.8%)	3 (17.6%)	10 (35.7%)	5 (22.7%)	2 (25%)
Progressive disease	39 (39.4%)	9 (39.1%)	8 (47.1%)	8 (28.6%)	11 (50%)	3 (37.5%)
Not evaluable	8	3	1	2	1	1
Response rate	31.3%	26.1%	35.3%	35.7%	27.3%	37.5%
Disease control rate	59.6%	60.9%	52.9%	71.4%	50%	62.5%
Duration of ICI treatment (months)						
median	3.3	2.8	3.0	3.3	3.9	4.7
range	0.1 - 28.7	0.1-28.7	0.1-12.7	0.1-20.7	0.9-22.2	0.1-15.3
Duration of response						
median	15.4	NR	13.1	10.4	15.2	12.1
95%CI	(12.6 - NR)	(12.6 - NR)	(7.6 - NR)	(4.6 - NR)	(7.0 - NR)	(8.4 - NR)
PFS (months)						
median	4.7	5.3	4.9	4.9	2.2	7.6
95%CI	(2.3 - 7.4)	(2.1 - NR)	(2.3 - NR)	(2.0 - 11.4)	(1.7 - 15.2)	(2.3 - NR)
6-months PFS	42.6%	48.0%	46.1%	39.6%	33.3%	53.3%
95%CI	(33.8% - 53.7%)	(31.9% - 72.2%)	(26.4% - 80.5%)	(25.1% - 62.6%)	(18.2% - 61.0%)	(28.2% - 100%)
12-months PFS	28.0%	39.1%	24.6%	22.2%	22.9%	26.7%
95%CI	(20.0% - 39.2%)	(23.7% - 64.4%)	(8.4% - 71.6%)	(10.4% - 47/3%)	(10.2% - 51.2%)	(8.3% - 85.8%)
OS (months)						
median	16.2	22.5	12.0	13.4	20.4	NR
95%CI	(12.0 - 24.0)	(8.3 - NR)	(6.8 - NR)	(9.4 - NR)	(9.3 - NR)	(26.8 - NR)
12-months OS	58.8%	53.4%	44.0%	59.0%	63.7%	88.9%
95%CI	(49.5 - 69.7)	(36.3% - 78.7%)	(25.0% - 77.3%)	(43.3% - 80.2%)	(46.4% - 87.6%)	(70.6% - 100%)

**Table 3:** Efficacy results in the entire cohort and according to molecular subgroup

	Total (n=107)	PD-L1 unknown (n=62)	PDL1 negative (n=11)	PDL1 positive (n=34)	PDL1 ≥50% (n=25)
Best response to immunotherapy					
Partial response	31	17	4	10	9
Stable disease	28	17	2	9	7
Progressive disease	39	25	3	11	6
Not evaluable	8	2	2	4	2
Response rate	29.0%	28.3%	36.4%	29.4%	39.1%
Disease control rate	55.1%	56.7%	54.5%	55.9%	69.5%
Duration of immunotherapy (mo.)					
median	3.3	4.6	2.8	3.0	5.0
range	(0.1 - 28.7)	(0.5 - 23.9)	(0.1 - 28.7)	(0.1 - 12.7)	(0.7 - 15.3)
Duration of response (n=31)					
median	15.4	14.9	7.0	15.4	15.1
95%CI	(12.6 - NR)	(12.4 - NR)	(4.9 - NR)	(8.4 - NR)	(5.3 - NR)
PFS					
median	4.7	5.2	2.5	4.3	4.8
95%CI	(2.3 - 7.4)	(2.3 - 8.4)	(1.5 - NR)	(2.2 - 9.4)	(2.2 - NR)
6-months PFS	42.6%	46.5%	30.0%	39.9%	44.3%
95%CI	(33.8% - 53.7%)	(34.9% - 61.9%)	(11.6 - 77.3%)	(26.1% - 60.9%)	(27.9% - 70.3%)
12-months PFS	28.0%	28.4%	30.0%	25.0%	32.3%
95%CI	(20.0% - 39.2%)	(18.3% - 44.0%)	(11.6 - 77.3%)	(13.4% - 49.8%)	(17.0% - 61.3%)
OS					
median	16.2	15.9	11.7	35.8	35.2
95%CI	(12.0 - 24.0)	(11.8 - 23.6)	(6.8 - NR)	(9.3 - NR)	(13.2 - NR)
12-months OS	58.8%	60%	42.4%	60.4%	70.4%
95%CI	(49.5 - 69.7)	(48.7% - 73.9%)	(20.6% - 87.2%)	(43.4% - 84%)	(50.7% - 97.6%)

**Table 4:** Efficacy results according to PD-L1 status