

## **Supplementary Material**

### **Analysis of a real-world progression variable and related endpoints for patients with five different cancer types**

Aracelis Z. Torres<sup>1</sup>, Nathan C. Nussbaum<sup>1,2</sup>, Christina M. Parrinello<sup>1,3</sup>, Ariel B. Bourla<sup>1</sup>, Bryan E. Bowser<sup>1</sup>, Samuel Wagner<sup>4</sup>, David C. Tabano<sup>4</sup>, Daniel George<sup>5</sup>, Rebecca A. Miksad<sup>1</sup>

<sup>1</sup>Flatiron Health, Inc., New York, NY, USA; <sup>2</sup>New York University School of Medicine, New York, NY, USA; <sup>3</sup>Pine Mountain Consulting, LLC., Redding, CT, USA; <sup>4</sup>Bristol-Myers Squibb, Princeton, NJ, USA; <sup>5</sup>Duke University, Durham, NC, USA.

**Corresponding author:** Rebecca A. Miksad, MD, MPH; Flatiron Health, Inc., 233 Spring Street, Fifth Floor, New York, NY, 10025, ramiksad@flatiron.com

**Supplemental Table 1: rwEndpoint definitions**

	Index date	Event date	Censor date
<b>rwOS</b>	Start of 1L therapy <sup>a</sup>	Patient's date of death due to any cause	Last visit <sup>b</sup> or last abstracted oral episode of drug(s)
<b>rwPFS</b>		Date of first rwP event (abstracted) that occurs more than 14 days after index date or date of death, whichever occurs first.	Last unstructured clinic note assessed for rwP
<b>rwTTP</b>		Date of first rwP event (abstracted) that occurs more than 14 days after index date.	Last unstructured clinic note assessed for rwP
<b>rwTTD</b>		Last administration or non-cancelled order (IV drugs) or last abstracted oral episode of drug(s) contained in the index therapy. Permanent discontinuation was defined as meeting one of the following conditions: start of index therapy, a gap in treatment after the end of index therapy or death.	Last administration or non-cancelled order (IV drugs) or last abstracted oral episode of drug(s)
<b>rwTTNT</b>		Date of the start of line of therapy subsequent to index therapy or date of death, whichever occurs first.	Last visit <sup>b</sup>

<sup>a</sup>Index date was 2L therapy for the aMel cohort

<sup>b</sup>Visit categorized as vitals (any date on which a patient had a structured vitals measurement in the EHR); treatment (any date on which a patient had a structured medication administration in the EHR); lab (any date on which a patient had a structured lab in the EHR)

Abbreviations: 1L, first line; 2L, second line; aMel, advanced melanoma; EHR, electronic health record; IV, intravenous; rwOS, real-world overall survival; rwP, real-world progression; rwPFS, real-world progression-free survival; rwTTD, real-world time-to-discontinuation; rwTTP, real-world time-to-progression; rwTTNT, real-world time-to-next treatment.

**Supplemental Table 2: Baseline table for each analytic cohort by disease**

Table 2a: mBC cohort

<b>Characteristic</b>	<b>mBC cohort N=884</b>
<b>Age at metastatic diagnosis (years), median [IQR]</b>	64.0 [54.0;74.0]
<b>Age at metastatic diagnosis category (years), n (%)</b>	
<35	8 (0.9)
35–44	127 (14.4)
45–54	315 (35.6)
55–64	228 (25.8)
≥65	206 (23.3)
<b>Sex, n (%)</b>	
Female	870 (98.4)
Male	14 (1.6)
<b>Region, n (%)</b>	
Northeast	201 (22.7)
Midwest	149 (16.9)
South	315 (35.6)
West	161 (18.2)
Other/Missing	58 (6.6)
<b>Practice type, n (%)</b>	
Academic	44 (5.0)
Community	840 (95.0)

<b>Race, n (%)</b>	
White	607 (68.7)
Black	86 (9.7)
Asian	12 (1.4)
Other Race	126 (14.3)
Unknown/missing	53 (6.0)
<b>Stage at diagnosis, n (%)</b>	
Stage I	84 (9.5)
Stage II	216 (24.4)
Stage III	180 (20.4)
Stage IV	282 (31.9)
Stage not reported	122 (13.8)
<b>ER tested, n (%)</b>	868 (98.2)
<b>ER status among those tested, n (%)</b>	
Negative	225 (25.9)
Positive	642 (74.0)
Results unknown/not documented	1 (0.1)
<b>PR tested, n (%)</b>	868 (98.2)
<b>PR status among those tested, n (%)</b>	
Negative	344 (39.6)
Positive	485 (55.9)
Results unknown/not documented	39 (4.5)

<b>HER2 tested, n (%)</b>	841 (95.1)
<b>HER2 status among those tested, n (%)</b>	
Negative	650 (77.3)
Positive	148 (17.6)
Equivocal	33 (4.0)
Results unknown/not documented	10 (1.3)
<b>HR/HER2 status among those tested, n (%)</b>	
HR- and HER2+	45 (5.1)
HR+ and HER2-	508 (57.5)
HR+ and HER2+	100 (11.3)
Triple Negative	132 (14.9)
HR/HER2 status unknown/not documented	99 (11.2)
<b>First-line therapy class, n (%)</b>	
CDK4/6 inhibitor-based therapy	0 (0.0)
Chemo + HER2 targeted-based therapy	95 (10.7)
Chemotherapy	351 (39.7)
Clinical study drug-based therapies	3 (0.3)
Endocrine therapy	376 (42.5)
HER2 targeted-based therapy	32 (3.6)
mTOR inhibitor-based therapy	11 (1.2)
Other therapies	16 (1.8)
Abbreviations: CDK, cyclin-dependent kinase; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IQR, interquartile range; mBC, metastatic breast cancer; mTOR, mammalian target of rapamycin; PR, progesterone receptor.	

Table 2b: aMel cohort

	<b>aMel cohort N = 152</b>
<b>Age at advanced diagnosis (years), median [IQR]</b>	64.0 [56.0; 75.0]
<b>Age at advanced diagnosis category (years), n (%)</b>	
<35	7 (4.6)
35–44	16 (10.5)
45–54	56 (36.8)
55–64	32 (21.1)
≥65	41 (27.0)
<b>Sex, n (%)</b>	
Female	50 (32.9)
Male	102 (67.1)
<b>Region, n (%)</b>	
Northeast	24 (19.7)
Midwest	23 (15.8)
South	63 (41.4)
West	12 (7.9)
Other/Missing	30 (19.7)
<b>Practice type, n (%)</b>	
Academic	29 (19.1)
Community	123 (80.9)
<b>Race, n (%)</b>	
White	127 (83.6)

Black	1 (0.7)
Asian	0 (0.0)
Other Race	12 (7.9)
Unknown/Not Documented	12 (7.9)
<b>Stage at diagnosis, n (%)</b>	
Stage I	10 (6.6)
Stage II	33 (21.7)
Stage III	29 (19.1)
Stage IV	42 (27.6)
Group stage is not reported	38 (25.0)
<b>BRAF tested, n (%)</b>	147 (96.7)
<b>BRAF status among those tested, n (%)</b>	
Mutation negative	71 (48.3)
Mutation positive	75 (51.0)
Results unknown/not documented	1 (0.7)
<b>KIT tested, n (%)</b>	45 (29.6)
<b>KIT status among those tested, n (%)</b>	
Mutation negative	39 (86.7)
Mutation positive	5 (11.1)
Results unknown/not documented	1 (2.2)
<b>PD-L1 tested, n (%)</b>	10 (6.6)
<b>PD-L1 status among those tested, n (%)</b>	
PD-L1 negative/not detected	3 (30.0)
PD-L1 positive	2 (20.0)

Results unknown/not documented	2 (20.0)
No interpretation given in report	3 (30.0)
<b>NRAS tested, n (%)</b>	43 (28.3)
<b>NRAS status among those tested, n (%)</b>	
Mutation negative	33 (76.7)
Mutation positive	9 (20.9)
Results unknown/not documented	1 (2.3)
<b>First-line therapy class, n (%)</b>	
(Peg)interferon-based therapies	0 (0.0)
BRAF/MEK-based therapies	36 (23.7)
Chemotherapy only (single-agent or combos)	20 (13.2)
Clinical study drug-based therapies	2 (1.3)
Modified viral therapies	1 (0.7)
PD-1/PD-L1-based therapies	56 (36.8)
Yervoy + PD-1/PD-L1-based therapies	10 (6.6)
Yervoy-based therapies	22 (14.5)
Other therapies	5 (3.3)
Abbreviations: aMel, advanced melanoma; IQR, interquartile range; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1.	

Table 2c: SCLC cohort



	<b>SCLC cohort N=359</b>
<b>Age at initial diagnosis (years), median [IQR]</b>	68.0 [60.0;74.5]
<b>Age categories at initial diagnosis (years), n (%)</b>	
<35	1 (0.28)
35–49	16 (4.5)
50–64	125 (34.8)
≥65	217 (60.4)
<b>Sex, n (%)</b>	
Female	178 (49.6)
Male	181 (50.4)
<b>Region, n (%)</b>	
Northeast	81 (22.6)
Midwest	78 (21.7)
South	132 (36.8)
West	45 (12.5)
Other/Missing	23 (6.4)
<b>Practice type, n (%)</b>	
Academic	22 (6.1)
Community	337 (93.9)
<b>Race, n (%)</b>	
White	250 (69.6)
Black	25 (7.0)
Asian	1 (0.3)
Other Race	35 (9.7)

Unknown/missing	48 (13.4)
<b>Smoking status, n (%)</b>	
History of smoking	352 (98.1)
No history of smoking	7 (1.9)
Unknown/not documented	0 (0.0)
<b>Stage at diagnosis, n (%)</b>	
Stage I	10 (2.8)
Stage II	11 (3.1)
Stage III	58 (16.2)
Stage IV	199 (55.4)
Stage not reported	81 (22.6)
<b>SCLC-specific stage at diagnosis, n (%)</b>	
Extensive disease	231 (64.3)
Limited disease	105 (29.2)
Unknown/not documented	23 (6.4)
<b>Resection, n (%)</b>	
Yes	10 (2.8)
No/unknown	349 (97.2)
<b>Upfront radiation therapy, n (%)</b>	
Yes	123 (34.3)
No/unknown	236 (65.7)
<b>First-line therapy class, n (%)</b>	
Platinum + Etoposide	339 (94.4)
Other	19 (5.3)

Unknown/not documented	1 (0.3)
Abbreviations: IQR, interquartile range; SCLC, small cell lung cancer.	

Table 2d: mRCC cohort

	<b>mRCC cohort N=323</b>
<b>Age at metastatic diagnosis (years), median [IQR]</b>	66.0 [58.0;73.0]
<b>Age categories at metastatic diagnosis (years), n (%)</b>	
<35	2 (0.6)
35–49	14 (4.3)
50–64	125 (38.7)
≥65	182 (56.3)
<b>Sex, n (%)</b>	
Female	86 (26.6)
Male	237 (73.4)
<b>Region, n (%)</b>	
Northeast	56 (17.3)
Midwest	58 (18.0)
South	119 (36.8)
West	58 (18.0)
Other/Missing	32 (9.9)
<b>Practice type, n (%)</b>	
Academic	25 (7.7)
Community	298 (92.3)

<b>Race, n (%)</b>	
White	215 (66.6)
Black or African American	23 (7.1)
Asian	4 (1.2)
Other Race	48 (14.9)
Unknown/missing	33 (10.2)
<b>Smoking status, n (%)</b>	
History of smoking	202 (62.5)
No history of smoking	119 (36.8)
Unknown/Not documented	2 (0.6)
<b>Stage at diagnosis, n (%)</b>	
Stage I–III	124 (38.4)
Stage IV	189 (58.5)
Stage not reported	10 (3.1)
<b>Histology, n (%)</b>	
Clear Cell	225 (69.7)
Non-clear Cell	31 (9.6)
RCC, NOS	67 (20.7)
<b>Nephrectomy, n (%)</b>	
Yes, pre-metastatic	125 (38.7)
Yes, post-metastatic	75 (23.2)
Yes, date unknown	2 (0.6)
No	121 (37.5)
<b>First-line therapy class, n (%)</b>	

Anti-VEGF TKI	233 (72.1)
mTOR inhibitor	39 (12.1)
PD-1/PD-L1 therapy	14 (4.3)
Other therapies	37 (11.5)
Abbreviations: IQR, interquartile range; mRCC, metastatic renal cell carcinoma; mTOR, mammalian target of rapamycin; TKI, tyrosine kinase inhibitor; NOS, not otherwise specified; VEGF, vascular endothelial growth factor.	

Table 2e: aGEC cohort

	<b>aGEC cohort N=370</b>
<b>Age at advanced diagnosis date (years), median [IQR]</b>	67.0 [58.0;74.0]
<b>Age categories at advanced diagnosis date (years), n (%)</b>	
<35	2 (0.5)
35–49	28 (7.6)
50–64	133 (35.9)
≥65	207 (56.0)
<b>Sex, n (%)</b>	
Female	89 (24.1)
Male	281 (75.9)
<b>Region, n (%)</b>	
Northeast	28 (7.6)
Midwest	30 (8.1)
South	152 (41.1)
West	160 (43.2)

Other/missing	0 (0.0)
<b>Practice type, n (%)</b>	
Academic	0 (0.0)
Community	370 (100.0)
<b>Race, n (%)</b>	
White	264 (71.4)
Black or African American	24 (6.5)
Asian	9 (2.4)
Other Race	28 (7.6)
Unknown/missing	45 (12.2)
<b>Smoking status, n (%)</b>	
History of smoking	264 (71.4)
No history of smoking	106 (28.6)
Unknown/Not documented	0 (0.0)
<b>Stage at diagnosis, n (%)</b>	
Stage I	18 (4.9)
Stage II	66 (17.8)
Stage III	75 (20.3)
Stage IV	176 (47.6)
Stage not reported	35 (9.5)
<b>Disease site, n (%)</b>	
Esophageal	175 (47.3)
Gastric	112 (30.3)
Gastroesophageal Junction	83 (22.4)

<b>Histology, n (%)</b>	
Adenocarcinoma	306 (82.7)
Adenosquamous	3 (0.8)
Squamous Cell Carcinoma	58 (15.7)
Other	2 (0.5)
Unknown/Not Documented	1 (0.3)
<b>Surgery status, n (%)</b>	
Surgery on or before index	55 (14.9)
Unknown surgery date	0 (0.0)
No surgery on or before index	315 (85.1)
<b>HER2 tested, n (%)</b>	233 (63.0)
<b>HER2 status among those tested, n (%)</b>	
Positive	42 (18.0)
Negative	178 (76.4)
Equivocal	4 (1.7)
Results unknown/not documented	9 (3.9)
<b>First-line therapy class, n (%)</b>	
Chemo mono or combination	317 (85.7)
Anti-VEGF +/- chemo-based	8 (2.2)
HER2 +/- chemo-based	28 (7.6)
Clinical study drug-based	12 (3.2)
Other therapies	5 (1.4)
Abbreviations: aGEC, advanced gastric/esophageal cancer; HER2, human epidermal growth factor receptor 2; IQR, interquartile range; VEGF, vascular endothelial growth factor.	