PATIENTS LOST TO PRECISION TREATMENT DUE TO SUBOPTIMAL TESTING:US AND EU REAL WORLD EVIDENCE

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Introduction

The number of personalized medicines has increased steadily since 2008 and is now standing at 132, with 42% of all new drugs in development, including 73% of all new oncology drugs, being personalized medicines[1]. It is estimated that $200bn of therapy revenue is dependent on the use of diagnostics[2], with 60%-70% of clinical decisions based on the results of diagnostics[3].
As healthcare delivery shifts towards outcome or value-based models4, it becomes increasingly important to assess the position of diagnostics, particularly companion diagnostics, that leverage generally higher value therapies within that new delivery paradigm. Diagnostics are often considered a low value addition to costs[3].
In 2015, a FDA/AACR/ASCO-sponsored workshop stated that: "The success of personalized medicine depends on having accurate, reproducible and clinically useful companion diagnostic tests to identify patients who can benefit from targeted therapies" 5. However, access to those tests will only be optimized if they are considered a positive contribution to the value equation. The objective of this work is to examine the effect of suboptimal testing on numbers of patients receiving specific personalized therapies and the consequent loss in revenue to pharma.

Methods

Diaceutics analysed real world (versus clinical trial setting) US testing data for 13 known oncology biomarkers, where the greatest experience in parallel test and therapy launches exists. Data gathered from laboratory partners, Centers for Medicaid Services (CMS) databases, SEER (Surveillance, Epidemiology and End Results) and the literature were used to populate an analytical framework constructed in Microsoft Excel. The analytical framework quantified the number of patients likely missing out on the right therapy due to avoidable testing issues. To ensure a fully evidence-based assessment, we focused only on the basics of an efficient testing market: turnaround time, test sensitivity and sample management, where adequate published references of real-time testing gaps for each biomarker existed. We did not include quantification of the number of patients who should/could be tested (if there were faster test adoption at the physician and laboratory levels) although we speculate the likely impact on our analysis.

Results

Table 1 shows the selected biomarkers, an exemplar disease state associated with the biomarker and used for calculation of patient numbers and the prevalence of the biomarker in the selected patient population.

Table 2 shows the predominant test platform used to assay the biomarker and proportion of patients lost to an actionable test result.

Table 3 shows the proportion of actionable test results lost as a result of test inefficiencies calculated as the sum of test loss factors multiplied by the number of tests being performed.

Table 4 shows the number of patients with lost actionable results per month per biomarker calculated as the test volume multiplied by the prevalence of the biomarker (i.e. actionable test result) multiplied by the test losses. It also shows the calculated number of missed personalized therapies (i.e. therapy actioned by an appropriate test result).

Missed treatments were assigned a $/month revenue value based on average treatment cost per patient for the personalized therapy associated with the biomarker-condition pair (**Table 5**).

BIOMARKER	EXEMPLAR DISEASE ASSOCIATED WITH BIOMARKER	ANNUAL INCIDENCE METASTATIC DISEASE (US DATA)	PREVALENCE OF BIOMARKER IN TARGET POPULATION
HER2	BREAST CANCER	213745	0.25
PD-L1	NSCLC	33256	0.44
VEGF	CRC	33622	0.25
EGFR	NSCLC	33256	0.2
MET	OVARIAN	11363	0.091
ALK	NSCLC	33256	0.07
BRAF	MALIGNANT MELANOMA	56720	0.35
BRCA	BREAST CANCER	213745	0.1
RAS	PANCREATIC CANCER	26535	0.01
KRAS	CRC	33622	0.1617
IDH2	CLL	14400	0.0922
FLT3	AML	14000	0.263
JAK 2	AML	14000	0.0065

Table 1. Details of selected biomarkers

BIOMARKER	PREDOMINANT TEST PLATFORM	LOSS FACTOR		
		% TAT ABOVE 5 DAYS	% FALSE NEGATIVES FROM THIS TYPE OF TEST	% SAMPLE FAILURE FROM THIS TYPE OF TEST (TEST DOES NOT HAPPEN)
HER2	IHC, FISH	0.05	0.3	0.1
PD-L1	IHC	0.32	0.3	0.02
VEGF	ELISA	0.05	0.3	0.02
EGFR	PCR	0.05	0.2	0.05
MET	IHC, FISH	0.05	0.2	0.02
ALK	FISH	0.05	0.1	0.08
BRAF	PCR,SEQUENCING	0.05	0.39	0.1
BRCA	SEQUENCING	0.05	0.34	0.22
RAS	PCR, SEQUENCING	0.05	0.14	0.22
KRAS	PCR, SEQUENCING	0.05	0.02	0.22
IDH2	PCR	0.05	0.03	
FLT3	PCR	0.05	0.29	0.05
JAK 2	PCR			

Table 2. Test platforms and associated patient losses for selected biomarkers

BIOMARKER	DISEASE ASSOCIATED WITH BIOMARKER	% OF TESTING EFFICIENCY (Proportion of tests giving an actionable result)	CALCULATED PROPORTION OF TESTS LOST DUE TO TEST INEFFICIENCIES
HER2	BREAST CANCER	0.55	0.45
PD-L1	NSCLC	0.36	0.64
VEGF	CRC	0.63	0.37
EGFR	NSCLC	0.70	0.30
MET	OVARIAN	0.73	0.27
ALK	NSCLC	0.77	0.23
BRAF	MALIGNANT MELANOMA	0.46	0.54
BRCA	BREAST CANCER	0.39	0.61
RAS	PANCREATIC CANCER	0.59	0.41
KRAS	CRC	0.59	0.41
IDH2	CLL	0.71	0.29
FLT3	AML	0.92	0.08
JAK 2	AML	0.61	0.39

Table 3. Calculated proportions of biomarker tests lost due to test inefficiencies

BIOMARKER	DISEASE ASSOCIATED WITH BIOMARKER	CALCULATED PATIENTS MISSED PER MONTH DUE TO POOR TESTING EFFICIENCY	PROPORTION OF PATIENTS RECEIVING PERSONALIZED THERAPY*	CALCULATED PATIENTS NOT TREATED PER MONTH
HER2	BREAST CANCER	1995	0.84	1675
PD-L1	NSCLC	3349	0.84	2813
VEGF	CRC	66	0.84	55
EGFR	NSCLC	268	0.84	225
MET	OVARIAN	20	0.84	16
ALK	NSCLC	99	0.84	83
BRAF	MALIGNANT MELANOMA	1080	0.84	907
BRCA	BREAST CANCER	457	0.84	383
RAS	PANCREATIC CANCER	4	0.84	3
KRAS	CRC	293	0.84	246
IDH2	CLL	25	0.84	21
FLT3	AML	50	0.84	42
JAK 2	AML	23	0.84	19

Table 4. Calculated patients missed and patients not treated due to test inefficiencies
*: Patients receiving a therapy based on the result of the biomarker test

BIOMARKER	DISEASE ASSOCIATED WITH BIOMARKER	CALCULATED PATIENTS NOT TREATED PER MONTH	REVENUE PER PATIENT	CALCULATED TOTAL MONTHLY REVENUE LOST TO TESTING INEFFICIENCY
HER2	BREAST CANCER	1675	$55,687	$93,275,725
PD-L1	NSCLC	2813	$150,000	$421,950,000
VEGF	CRC	55	$33,500	$1,842,500
EGFR	NSCLC	225	$72,000	$16,200,000
MET	OVARIAN	16	$49,000	$784,000
ALK	NSCLC	83	$11,570	$960,310
BRAF	MALIGNANT MELANOMA	907	$100,000	$90,700,000
BRCA	BREAST CANCER	383	$135,000	$51,705,000
RAS	PANCREATIC CANCER	3	$72,000	$216,000
KRAS	CRC	246	$35,000	$8,610,000
IDH2	CLL	21	$95,230	$1,999,830
FLT3	AML	42	$95,230	$3,999,660
JAK 2	AML	19	$95,230	$1,809,370

Table 5. Calculated monthly revenue losses due to test inefficiencies

Calculations indicate:

- 6488 patients/month (77856/year) lost to therapy
- Revenue losses to pharma $694m/month ($8328m/year)

Conclusions

1. Test inefficiencies have the potential to significantly reduce the number of patients receiving personalized therapy with associated losses in revenue to pharma.
2. The estimate of patients lost to therapy represents nearly 30% of the oncology market in the US and the situation in the EU5 is likely to be similar, with an estimatedtotal loss of >$16bn/year.
3. The estimates are likely underestimates as test adoption (i.e. whether the patient with the condition receives the biomarker test) is not included in the calculations, neither are costs due to failed treatments.
4. Test performance is the greatest contributor to patient losses, therefore the factor whose optimisation produces the greatest increase in patients being tested and treated. For example, a 10 percentage points increase in IHC sensitivity for HER2 would provide an additional 4476 patients and $248m revenue per year.
5. Test performance factors beyond simple test availability need to be considered as part of the matrix of elements contributing to value calculations for outcome-based pricing models[6].
6. Test optimisation, beyond simple availability, could help mitigate falling returns on new drugs, a factor which could potentially limit pharma's traditionally high levels of innovation[7].

References

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