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Comprehensive Characterization of Solid Tumor Immune Profiles for Precision Immunotherapy Using Immune Report Card℠

The right drug or right trial…
For Every Patient

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Introduction

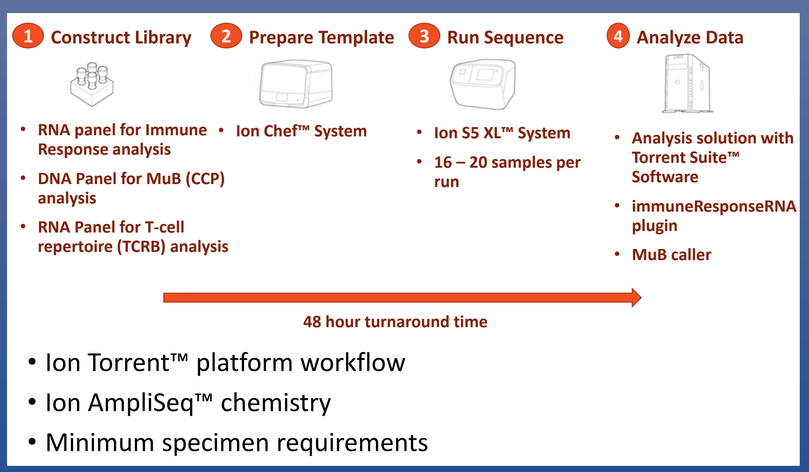
Monoclonal antibodies directed at inhibitory immune receptors have emerged as successful treatment options for numerous tumor types using both mono and combination modalities. However, response rates are low (20-30%) for current FDA approved checkpoint inhibitors, and better predictive markers are needed to support patient selection for treatment. **We present findings from patients tested by Immune Report Card℠, a validated NYS CLEP approved clinical assay that measures markers of checkpoint inhibitor response and targets in immunotherapeutic clinical trials for appropriate treatment selection.**

Methods

306 FFPE samples in 30 solid tumor types (including 163 patients across 12 tumor types with FDA approvals for checkpoint inhibitors) were comprehensively evaluated by Immune Report Card for markers of response to checkpoint inhibitors including:

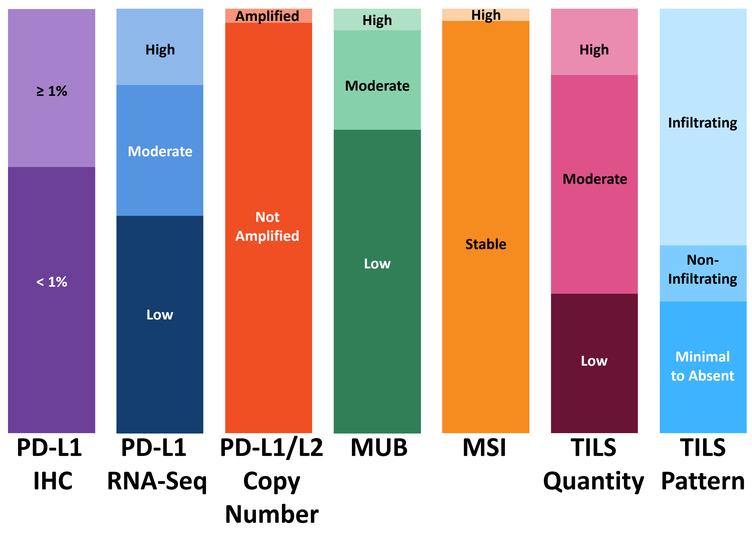
- **PD-L1** pathway activation by IHC, RNA-Seq and copy number/amplification
- Genomic instability using **microsatellite instability (MSI)** by PCR and **mutational burden (MUB**) by DNA-Seq.
- **Tumor infiltrating lymphocytes (TILS**) expression by IHC and quantity by RNA-Seq to characterize **"hot" (overexpression of CD8 and infiltrating or excluded TILS pattern)** and **"cold" tumors**
- **20 therapeutic targets in clinical development**.

Workflow



- Ion Torrent™ platform workflow
- Ion AmpliSeq™ chemistry
- Minimum specimen requirements

Immune Response Markers



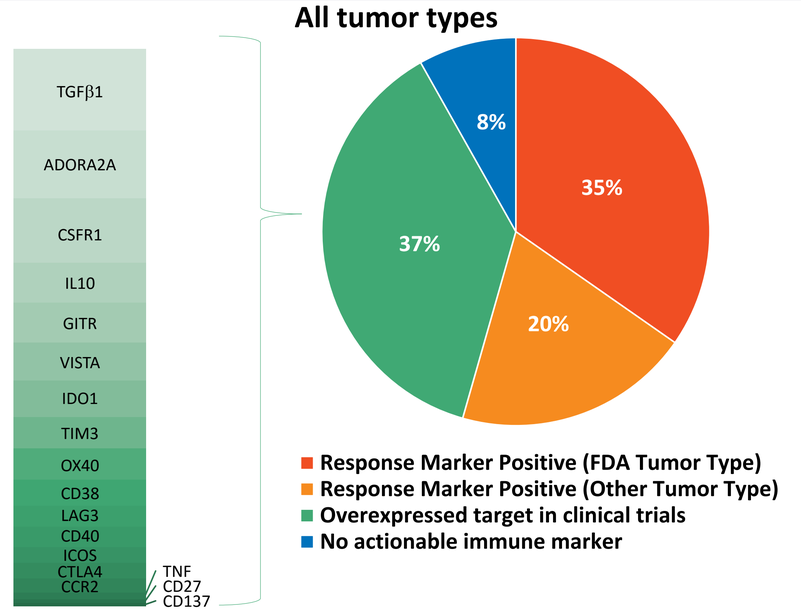
- **160 (52%) patients harbor at least one response marker with 77 (25%) having >1 response marker.**
- **64/114 (56%) of PD-L1 IHC+ cases have >1 response marker**
- **43 (14%) are "hot" tumors with most cases (62%) in tumors with FDA approved checkpoint inhibitors**

Immunotherapeutic Trials

Target	Unique Trials	Unique Patients	Therapies (Single and/or Combination)
ADORA2A	3	97	AZD4635; CPI-444; PBF-509
CCR2	2	11	Plozalizumab; BMS-813160; CCX872-B; PF-04136309
CD137	6	50	Urelumab; Utomilumab
CD27	1	24	Varlilumab
CD38	3	62	Daratumumab
CD40	11	53	ADC-1013; APX005M; CP-870,893; RO7009789; SEA-CD40
CSF1R	13	113	Cabiralizumab; Emactuzumab; AMG 820; BLZ945; LY3022855; PD-0360324; PLX73086
CTLA4	108	42	Ipilimumab; Tremelimumab; AGEN1884; BMS-986218; MK-1308
GITR	7	82	BMS-986156; GWN 323; INCAGN01876; MEDI1873; MK-4166; TRX518
ICOS	2	60	GSK3359609; JTX-2011
IDO1	17	87	Epacadostat; Indoximod; BMS-986205; GDC-0919; KHK2455; PF-06840003
IL10	1	64	MK-1966
LAG3	11	53	BI 754111; BMS-986016; LAG525; MGD013; MK-4280; REGN3767; TSR-033
OX40	10	60	BMS-986178; GSK3174998; INCAGN01949; MEDI0562; MEDI6383; MEDI6469; MOXR0916; PF-04518600
PD-1	404	73	Nivolumab; Pembrolizumab; AGEN2034; BGB-A317; BI 754091; JNJ-63723283; MEDI0680; MGD013; PDR001; PF-06801591; REGN2810; TSR-042
PD-L1	157	73	Atezolizumab; Avelumab; Durvalumab; CA-170; CX-072; FAZ053; KN035; LY3300054
TGFB1	2	122	Fresolimumab; NIS793
TIM3	3	49	LY3321367; MBG453; TSR-022
TNF	1	21	Certolizumab
VISTA (B7-H5)	2	67	CA-170

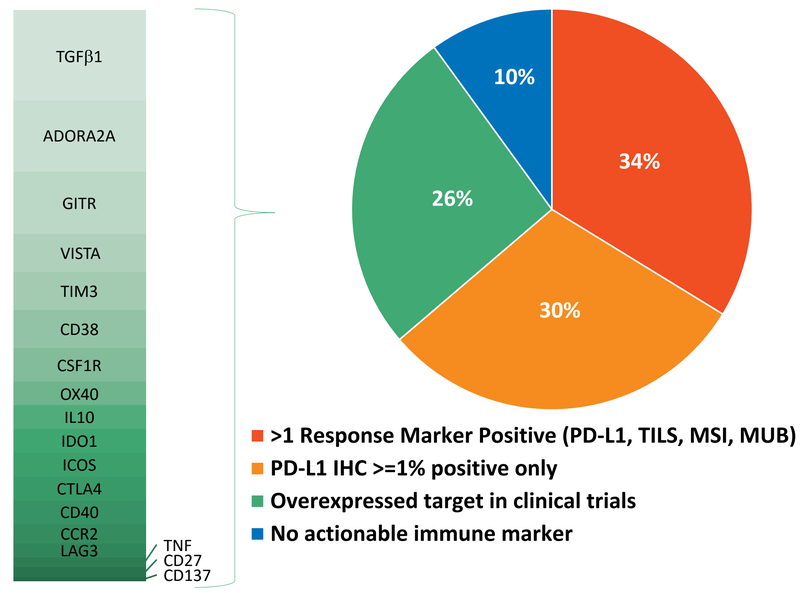
Arm-specific clinical trial matching provides options for all patients who either do not have at least one known marker of response or who are seeking second line treatment

Actionability



On and off-label actionability across 30 tumor types

Tumor types with FDA approved checkpoint inhibitors



Clinical trials may be more appropriate for some patients eligible for checkpoint inhibitors.

Conclusions

As checkpoint inhibition moves from treatment of last resort to first and second line therapy, Immune Report Card provides actionable results for the total tumor immune microenvironment, including:

Frontline Response Markers for Checkpoint Inhibition:

- **On/Off-Label:** PD-L1 IHC (22C3, 28-8, SP142), MSI, MUB
- **Additional Evidence:** PD-L1 RNA-Seq, PD-L1/L2 copy number, TILS pattern and expression (hot vs. cold tumors)

Subsequent Therapy Planning :

- **Overexpressed immunotherapeutic targets for optimal selection of combination therapy in clinical trials**