The DGP-QUIP PD-LI

and

TMB EQA program

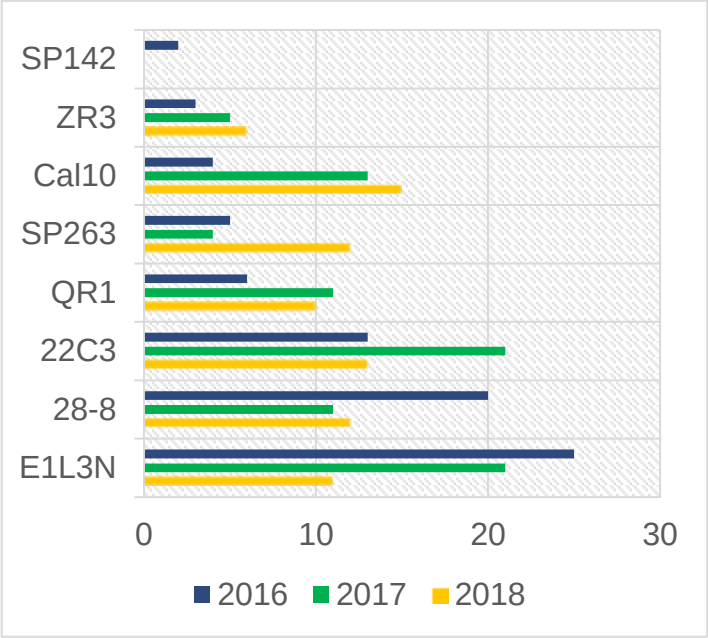
Manfred Dietel

PD-L1 activities 2016-2019

- Since 2016: 5 PD-L1 proficiency tests
  - 3 NSCLC
  - 1 Malignant Melanoma
  - 1 Urothelial Carcinoma
- Live trainings
- Online trainings (webinar + webcast)
- PD-L1 Website

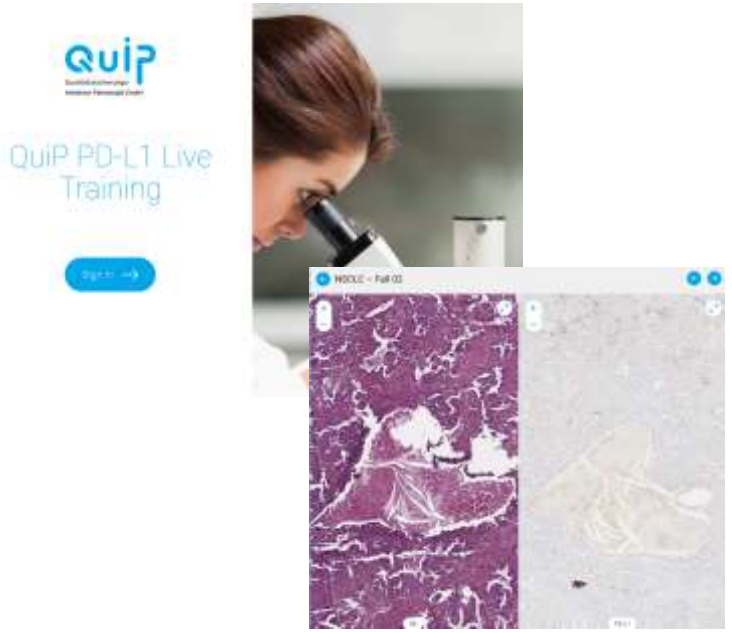
PD-L1 NSCLC: Used antibodies

AK	2016	2017	2018
E1L3N	25	21	11
28-8	20	11	12
22C3	13	21	13
QR1	6	11	10
SP263	5	4	12
Cal10	4	13	15
ZR3	3	5	6
SP142	2	0	0



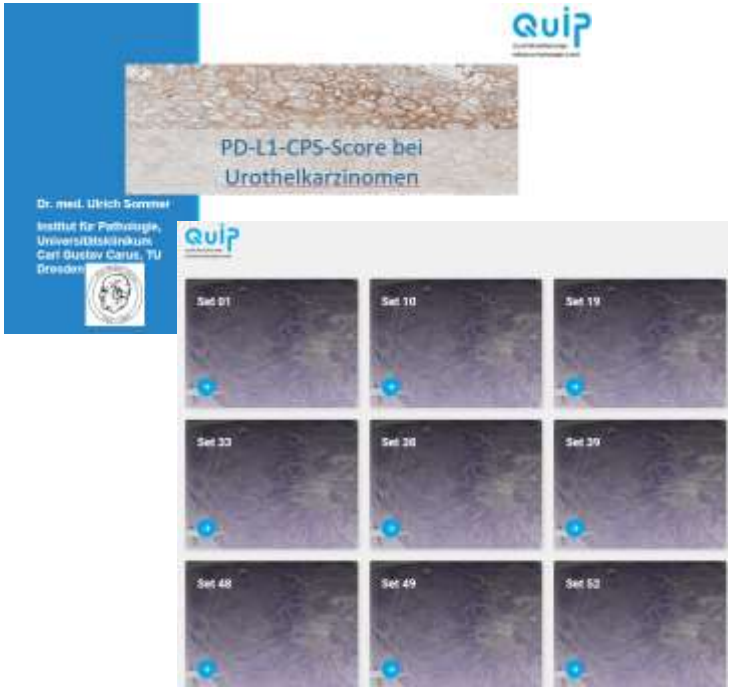
Live training with digital scoring

- Since 2016 3 live trainings in Berlin
- 2016/2017 focus on NSCLC
- 2018 including Urothelial Carcinoma and HNSC
- Since 2018 with digital scoring and digital TED-voting (tablets)
- 3-5 speakers with different specialisations



Webinar/Webcasts

- 2 different types
  - As a training before a proficiency test:
    - explanation of scores and cutoffs
    - Possible pitfalls
    - Training of example cases –live microscopy and virtual TED vote
  - As a feedback tool after a proficiency test:
    - Scan of all participants slides
    - Analysis of actual pitfalls
    - Antibody analysis
    - live microscopy of anonymous participant slides

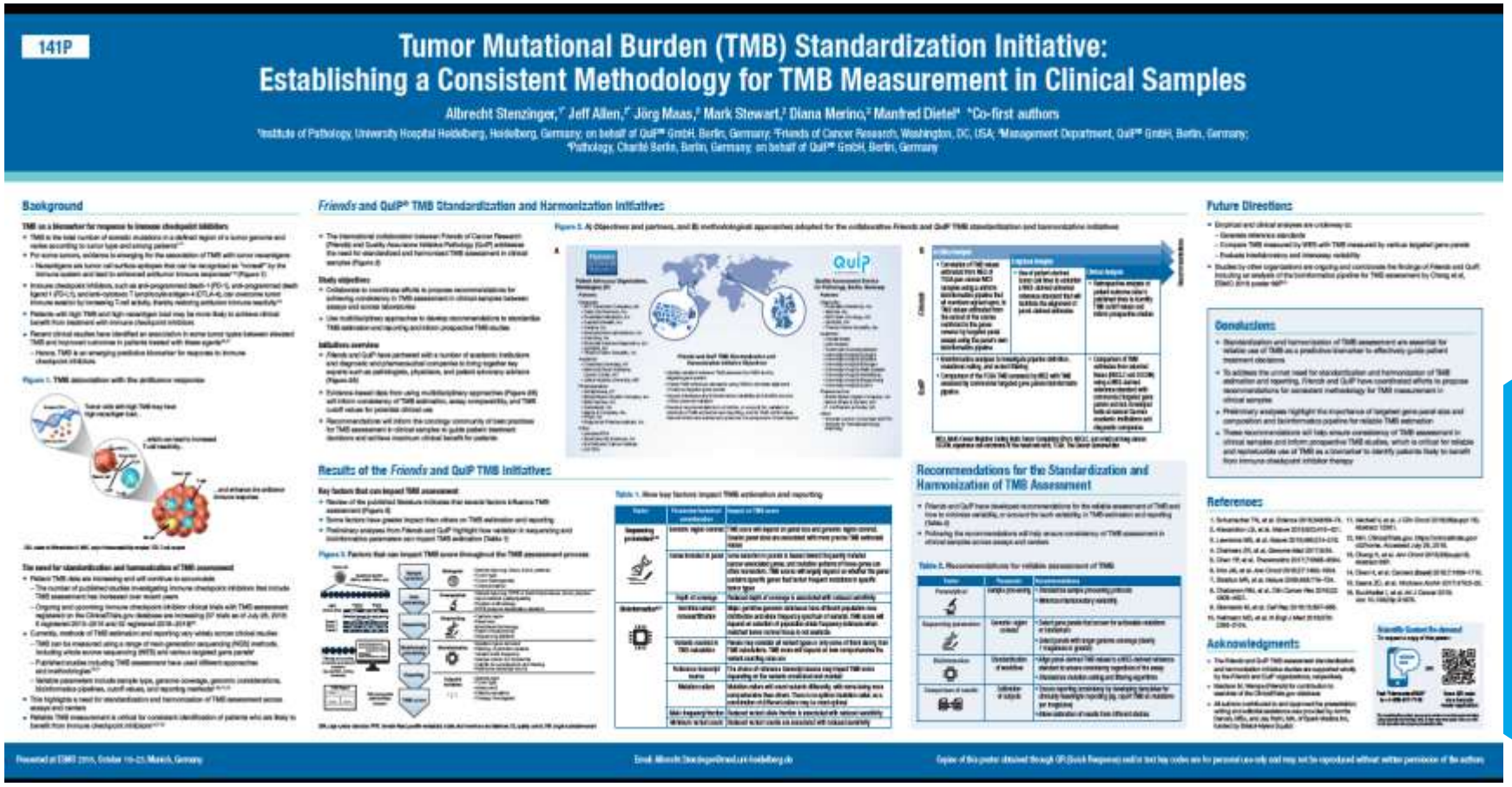


TMB assessment: Two independent efforts to harmonize assays and align standards

- Participating organisations:
  - **Pharma:** BMS, MSD, Roche
  - **Diagnostic companies:** Ilumina, NEO New Oncology, Qiagen, Thermo Fisher Scientific, Foundation Medicine

- Participating organisations:
  - **Pharma:** AstraZeneca, BMS, EMD Serono, Genentech, MSD, Pfizer
  - **Diagnostic companies:** ACT Genomics, Foundation Medicine, Guardant Health, Illumina, NeoGenomics, OmniSeq, PGDx, Qiagen, Thermo Fisher Scientific
  - **Others:** FDA, MSKCC, NCI

These initiatives collectively aim to better understand the parameters used for TMB assessment, establish standards, and compare existing assays to understand how they relate to one another



A. Stenzinger et al. ESMO 2018 Abstract 141P

Overview on Test Approach – Technical Comparability Study

Included TMB panels (sorted by company):

* **ThermoFisher Assay:** Oncomine Tumor Mutation Load Assay

* **Qiagen** **„TMB-Panel“** QIAseq Targeted DNA IO Panel (12); **“MSI booster panel”** QIAseq Targeted DNA Booster Panel (96)

* **NEO New Oncology:** NEOplus v2 RUO

* **Illumina:** Illumina TruSight™ Oncology 500 (TSO500)

* **Foundation Medicine:** FoundationOne (F1) Panel

Panels assessed by test centers

Test centers	Panel 1st run	Panel 2nd run	Panel 3rd run
Charité Hospital Berlin	ThermoFisher	Qiagen	
University Hospital Dresden	Qiagen		
University Hospital Erlangen	Illumina	Qiagen	Academic (Agilent)
University Hospital Halle		Neo NewOncology	
Hambur, Inst. for Hematopathology	Neo NewOncology		
University Hospital Heidelberg	Illumina	ThermoFisher	Academic (Agilent)
University Hospital Cologne	Illumina	Neo NewOncology	Academic (Agilent)
Technical University of Munich	Illumina	ThermoFisher	
LM University of Munich		ThermoFisher	
University of Regensburg	Neo NewOncology	Qiagen	
University Hospital Zurich		F1	

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RESEARCH ARTICLE

Tumor mutational burden standardization initiatives: Recommendations for consistent tumor mutational burden assessment in clinical samples to guide immunotherapy treatment decisions

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QuIP
Quality in Pathology

Preliminary data analyses showed a considerable interassay complexity with assay and tumor type specific characteristics. This means that a harmonization and conversion of different assays as well as an adaptation to different tumor types – i.e. there is no tumor-agnosticity - is essential to get reliable and reproducible results.

Center; Johns Hopkins University; Columbia University; Thermo Fisher Scientific Inc; SeraCare Life Sciences Inc; Regeneron Pharmaceuticals Inc; QIAGEN NV; Pfizer Inc; Personal Genome Diagnostics (PGDx) Inc; OmniSeq LLC; NeoGenomics Laboratories Inc; Merck & Company Inc; Illumina Inc; Guardant Health Inc; Genentech Inc; Foundation Medicine Inc; EMD Serono Inc; Caris Life Sciences Inc; AstraZeneca LP; ACT Genomics Company Ltd; Bristol-Myers Squibb Company Inc

be followed to minimize variability in TMB estimation and reporting, which will ensure reliable and reproducible identification of patients who are likely to benefit from immune checkpoint inhibitors.

KEYWORDS

biomarkers, immune checkpoint inhibitors, neoantigens, next-generation sequencing, tumor mutational burden/load

IQN Path Selects SeraCare Life Sciences for First-Ever Tumor Mutational Burden External Quality Assessment Program

Posted on March 27, 2019

International expert group focused on improving quality of clinical biomarker testing launching pilot TMB proficiency program in Spring 2019

SeraCare Life Sciences, a manufacturer and leading partner to global in vitro diagnostics manufacturers and clinical laboratories, announced today their successful selection as a technology partner in support of the first ever tumor mutational burden (TMB) external quality assessment (EQA) program being developed by the International Quality Network for Pathology (IQN Path). Under the agreement with IQN Path, SeraCare Life Sciences will develop, manufacture, and supply a range of highly-characterized cell line genomic DNA and formalin-fixed, paraffin embedded (FFPE) standards with confirmed low, mid, and high levels of mutational burden within their exome regions. Beginning in June 2019, this material will be sent to about 30 labs as part of the first-ever EQA program for clinical labs who are monitoring TMB as part of their cancer tumor profiling assays by next-generation sequencing (NGS).

Studies to understand the clinical utility of TMB as a biomarker by NGS have been hampered by the lack of available standards and cost-effective assays for laboratories to implement. Last fall, SeraCare entered this space by joining the Friends of Cancer Research consortium on TMB harmonization as a key partner and provided standards for their harmonization efforts. Interest in TMB standards and harmonization is currently a very important topic of clinical research, as numerous pharma companies have clinical immuno-oncology (I-O) programs and seek to accurately and consistently assess TMB scores using NGS panels deployed in labs around the world in order to direct I-O therapeutics.