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Leading a new era of precision oncology

TMLA

TUMOUR MUTATION LOAD FOR
IMMUNOTHERAPY

Lead Clinical Scientist: -

Clinical Scientist: -

ONC19	-	Requester	-
Surname	-	Contact details	-
Forename	-	Date requested	-
DOB	-		
Gender	-	Tumour %	-
Histology #	-	Tumour %	-
Primary site	-	(macrodissected)	
Tumour subtype	-		
Tissue Type	-		

Comment:

The Oncofocus Tumor Mutation Load Test is a next-generation sequencing (NGS) assay that targets 409 genes spanning 1.7Mb of the genome to accurately provide an assessment of Mutation Load (mutations/Mb). The test is designed to select patients most likely to respond to immunotherapies.

Clinically Significant Biomarkers

■ Indicated ■ Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
<i>Tumor Mutational Burden</i> 22.68 Mut/Mb measured	Clinical trials and/or off-label	■ ipilimumab + nivolumab nivolumab	10

Sources included in relevant therapies: EMA1, FDA2, ESMO, NCCN

QC acceptance criteria: Average coverage >300, SNPs consistent with deamination 80%

Relevant Therapy Summary

● In this cancer type
 ○ In other cancer type
 ● In this cancer type and other cancer types
 ⊘ Contraindicated
 ⚠ Both for use and contraindicated
 ✕ No evidence

Tumor Mutational Burden

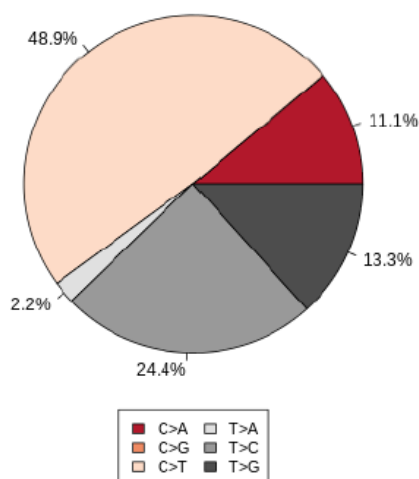
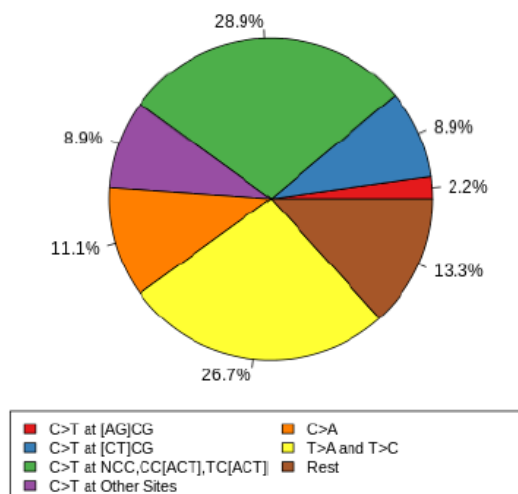
Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
ipilimumab + nivolumab	✕	✕	○	○	● (II)
nivolumab	✕	✕	✕	○	● (II)
atezolizumab	✕	✕	✕	✕	● (II)
BAT 1306 + aspirin, BAT 1306 + celecoxib	✕	✕	✕	✕	● (II)
durvalumab + tremelimumab	✕	✕	✕	✕	● (II)
ipilimumab + nivolumab, nivolumab	✕	✕	✕	✕	● (II)
ipilimumab + nivolumab, pembrolizumab	✕	✕	✕	✕	● (II)
sintilimab	✕	✕	✕	✕	● (I/II)
BI 754091 + BI 754111	✕	✕	✕	✕	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

ONC19:-
Referring pathology dept: -

www.oncologica.com

Disclaimer: The data presented here is a result of the curation of published data sources, but may not be exhaustive. The data version is 2019.03(009).

Substitution Type of Somatic Mutations

Signature Pattern of Somatic Mutations

Additional information:

High C>T at CpG is consistent with Spontaneous deamination of 5-methylcytosine (RED BLUE)¹

High C>T at CpC, CpC, TpC, T>A, and T>C is consistent with UV damage (BLUE GREEN YELLOW)²

High C>A is consistent with smoking damage (ORANGE)³

High C>T (site independent) is consistent with FFPE processing (GREEN PURPLE)⁴

¹Alexandrov LB et al. Nature. 2013; ²Hayward NK et al. Nature. 2017; ³Alexandrov LB et al. Cancer Etiology. 2016; ⁴Wong SQ et al. BMC Medical Genomics. 2014;

Relevant Therapy Details
Current ESMO Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

ESMO information is current as of 2018-11-16. For the most up-to-date information, search www.esmo.org.

Tumor Mutational Burden
☐ **ipilimumab + nivolumab**

Cancer type: Non-Small Cell Lung Cancer

Variant class: Tumor Mutational Burden

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Stage IV Squamous and Non-squamous Cell Carcinoma (First-line) (Not EMA-approved)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

Lead Clinical Scientist: -

Clinical Scientist: -

Current NCCN Information

☒ In this cancer type ☐ In other cancer type ☐ In this cancer type and other cancer types ☐ Contraindicated ☐ Not recommended ☐ Resistance

NCCN information is current as of 2018-11-16. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

Tumor Mutational Burden☐ **ipilimumab + nivolumab**

Cancer type: Non-Small Cell Lung Cancer

Variant class: Tumor Mutational Burden

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

☐ **nivolumab**

Cancer type: Non-Small Cell Lung Cancer

Variant class: Tumor Mutational Burden

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

Lead Clinical Scientist: -

Clinical Scientist: -

Current Clinical Trials Information

Clinical Trials information is current as of 2018-12-03. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

Tumor Mutational Burden

No NCT ID - see other identifier(s)

A Multicenter Phase II Study Of
Nivolumab Monotherapy In Recurrent
And/Or Metastatic Gastrointestinal
Cancer Patients With High Tumor
Mutation Burden (TMB-H)

Cancer type: Colon Cancer

Variant class: Tumor Mutational Burden

Other identifiers: TMB-H basket, UMIN000033182

Population segments: First line, Second line, Stage III, Stage IV

Phase: II

Therapy: nivolumab

Location: Japan

No NCT ID - see other identifier(s)

TR Accompanied with the Study Titled A
Multicenter Phase II Study of Nivolumab
Monotherapy in Recurrent and/or
Metastatic Gastrointestinal Cancer
Patients with High Tumor Mutation
Burden (TMB-H).

Cancer type: Colon Cancer

Variant class: Tumor Mutational Burden

Other identifiers: TMB-H basket TR, UMIN000033560

Population segments: Line of therapy N/A, Stage III, Stage IV

Phase: II

Therapy: nivolumab

Location: Japan

NCT02091141

My Pathway: An Open-Label Phase
IIa Study Evaluating Trastuzumab/
Pertuzumab, Erlotinib, Vemurafenib/
Cobimetinib, Vismodegib, Alectinib, and
Atezolizumab in Patients Who Have
Advanced Solid Tumors With Mutations
or Gene Expression Abnormalities
Predictive of Response to One of These
Agents

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: 1403013519, 2014-0459, AAAN9701, J1480, ML28897, ML28897/PRO
02, ML28897PRO/02, My Pathway, MyPathway, NCI-2014-01811, PRO 02

Population segments: BRCA, EGFR, Fourth line or greater, HER2 positive, Second line,
Stage III, Stage IV, Third line

Phase: II

Therapy: atezolizumab

Location: United States

US States: AR, AZ, CA, CO, FL, GA, IL, MD, MN, MO, NC, ND, NY, OH, OK, OR, PA, SD, TN,
TX, VA, WA, WI

Contact: Reference Study ID Number: ML28897 [888-662-6728; global-roche-genentech-trials@gene.com]

ONC19:-
Referring pathology dept: -

www.oncologica.com

Disclaimer: The data presented here is a result of the curation of published data sources, but may not be exhaustive. The data version is 2019.03(009).

Lead Clinical Scientist: -

Clinical Scientist: -

Date: 5 of 8

Tumor Mutational Burden (continued)

NCT03638297

PD-1 Antibody Combined With COX Inhibitor In MSI-H/dMMR Or High TMB Colorectal Cancer: A Single Arm Phase II Study

Cancer type: Colorectal Cancer

Variant class: Tumor Mutational Burden

Other identifier: GIHSYSU13

Population segments: First line, Second line, Stage IV

Phase: II

Therapies: BAT 1306 + aspirin, BAT 1306 + celecoxib

Location: China

NCT02029001

A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfilER

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: durvalumab + tremelimumab

Location: France

NCT03297606

Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: ipilimumab + nivolumab

Location: Canada

NCT03668119

A Randomized, Open-Label, Phase II Study of Nivolumab in Combination With Ipilimumab or Nivolumab Monotherapy in Participants With Advanced or Metastatic Solid Tumors of High Tumor Mutational Burden (TMB-H)

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: 16-71, BMS CA209-848, BMS Checkmate 848, CA209-848, CheckMate 848, CTRIAL-IE16-71, EudraCT Number: 2016-002898-35, U1111-1185-1326

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapies: ipilimumab + nivolumab, nivolumab

Locations: Australia, Italy, Romania

ONC19:-
Referring pathology dept: -

www.oncologica.com

Disclaimer: The data presented here is a result of the curation of published data sources, but may not be exhaustive. The data version is 2019.03(009).

Tumor Mutational Burden (continued)

NCT02693535

Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: NCI-2017-00510, Pro00014171, TAPUR

Population segments: (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapies: ipilimumab + nivolumab, pembrolizumab

Location: United States

US States: AL, AZ, CA, FL, GA, IL, MI, NC, ND, NE, OK, OR, PA, SD, TX, UT, VA, WA

Contact: Pam Mangat [pam.mangat@asco.org]

NCT03568539

An Open-label, Phase Ib Multicenter Study of IBI308 in Subjects With Advanced/ Metastatic Solid Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: CIBI308A102, NCI-2018-02011, UCI-18-19

Population segments: ALK, EGFR, Second line, Stage III, Stage IV

Phase: I/II

Therapy: sintilimab

Location: United States

US States: CA, GA, IN, MI, NV, NY, OK, SC, TX

Contact: Xiaolei Sun [213-182-0291; xiaolei.sun@innoventbio.com]

NCT03156114

An Open Label, Phase I Dose-finding Study of BI 754111 in Combination With BI 754091 in Patients With Advanced Solid Cancers Followed by Expansion Cohorts at the Selected Dose of the Combination in Patients With Non-small Cell Lung Cancer and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: 1381-0002, EudraCT Number: 2017-005042-29

Population segments: Second line, Stage III, Stage IV, Third line

Other inclusion criteria: MMR pathway underexpression

Phase: I

Therapy: BI 754091 + BI 754111

Locations: Canada, United States

US States: FL, OK, TN, WI

Contact: Boehringer Ingelheim [800-243-0127; clintriage.rdg@boehringer-ingelheim.com]

Tumor Mutational Burden (continued)**NCT03156114**

An Open Label, Phase I Dose-finding Study of BI 754111 in Combination With BI 754091 in Patients With Advanced Solid Cancers Followed by Expansion Cohorts at the Selected Dose of the Combination in Patients With Non-small Cell Lung Cancer and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: Tumor Mutational Burden

Other identifiers: 1381-0002, EudraCT Number: 2017-005042-29

Population segments: Second line, Stage III, Stage IV, Third line

Phase: I

Therapy: BI 754091 + BI 754111

Locations: Canada, United States

US States: FL, OK, TN, WI

Contact: Boehringer Ingelheim [800-243-0127; clintriage.rdg@boehringer-ingelheim.com]

Evidence Summary by Variant Class

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

Tumor Mutational Burden

Variant Class	Evidence Items
Tumor Mutational Burden	14

Report Authorised by

Signed



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