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## PROJECT AIM

The aim of COSMIC Actionability is to indicate the availability of drugs that target mutations in cancer and track the progress of clinical studies towards making new drugs available. Drugs that target somatic mutations are represented at all stages of drug development, through safety and clinical phases to market and repurposing, with additional case studies.

Clinical trials rarely identify variants at the DNA level, so all variants in Actionability are identified at the protein level. Trials are included in Actionability if:

1. Confirmation of a variant, expression, or predictive marker is a condition of patient recruitment

Or,

2. The trial details state the intention to correlate variant/expression with patient outcome. Once included in Actionability, all trial records are checked for updated details and results at every release until 10 years after the primary completion date.

## HOW TO OPEN AND NAVIGATE THE DOWNLOAD FILE

1. The Actionability Download file is in TSV format. It's likely that the file will open automatically in your default spreadsheet software, if not, launch the spreadsheet application and navigate to the downloaded file. The delimiters in the file are tabs, not spaces or commas.
2. Once the file is opened, navigate through the data by searching the tabular content, e.g. by National Clinical Trial ID (NCTID) or gene name (approved HUGO Gene Nomenclature Committee (HGNC) symbol).
3. Using a combination of filters may be useful if the result of your query is likely to be a list or involves searching data in more than one column:
  - A. In Excel, select the 'Data' tab followed by the 'Filter' button.
  - B. There will now be a button with a downward pointing arrow on the header row of every column. Click on any of these buttons to open a panel that displays a list of all the values present in the column, with a check box (tick mark) on the left side. By default, all values are selected (ticked).
  - C. To display individual values of interest, click the 'select all' check-box to unselect all values and re-select individual values of interest

## SOURCES OF DATA

Actionability content is manually curated from public clinical trial records, articles, conferences, labelling for marketed drugs, and company websites. Trial results are frequently published more than once, typically as interim results and later as a full record, with details of outcome measures that previously could not be calculated. Trial results available in a repository such as ClinicalTrials.gov often differ from published results or the corresponding clinical studies section of FDA drug labels. COSMIC aims to represent the most recent and/or complete results. The source of trial data is always indicated.

For trials with no results, the source identifies where the details of the trial were found. For trials with results, the source identifies where the results were obtained. Frequently, the source identifying the existence of the trial and the trial results are not the same; manual literature curation consistently identifies results for 40-50% more trials than are recorded in clinical trial repositories.

There are nine source types:

1. Pubmed
2. DOI
3. Unindexed journals, Conference abstracts
4. ClinicalTrials.gov
5. Corporate website
6. Submitted to clinicaltrials.gov
7. FDA drug label
8. EU clinical trials register
9. ANZCTR

For source types 1, 4, 6, Source will show the appropriate identifier. For source type 2, Source will show the DOI name. For source types 3, 5, 7, 8 and 9, Source shows the full URL

## DATA STRUCTURE SUMMARY

Actionability data is stored in a relational database with appropriate referencing to the core COSMIC database. The download file is the result of a selective export from the relational database.

Actionability has three principal units: drug, mutation, and disease. Mutations are cross-referenced to COSMIC core mutation records and thereby to a gene. These mutation instances are associated with one or more diseases using COSMIC's internal cancer classification scheme. Mutation-disease instances are associated with one or more drugs. The triple of drug-mutation-disease (DMD) indicates that a mutation has been associated with the effect of a drug in a specified cancer type. DMD instances are annotated with relevant data from clinical trials and case studies. Study details include the source of the data,, trial name, stage/phase of clinical development, primary completion date, number of patients, their treatment history, primary outcome measure and, where relevant, identity of the control. When the results of a trial are available they are recorded. If published results comment on whether the trial was successful or not, or the likelihood of progression, this is annotated as a Progression Remark.

## FULLY CURATED GENES

Content in Actionability is curated by gene. A gene is considered fully curated when every relevant trial systematically identified in clinical trial repositories and scientific literature has been added (for the latest list please see the Release Notes). For fully curated genes, searches are carried out at each release to identify new trials.

When a trial is added, all cohorts selecting or intending to correlate variants/expression with outcome measures are recorded, including those for genes that are not part of the fully curated set. Additional trials may exist for genes that are not fully curated.

## LINKING ACTIONABILITY RECORDS TO CORE COSMIC RECORDS

The download file contains genomic\_mutation\_IDs for single amino acid substitutions and some colocated variants. Similarly, fusion IDs can be linked to COSMIC fusion records. The disease nomenclature used in Actionability is a simplified version of the COSMIC classification system. The column Classification ID shows a COSO Identifier that allows linking to COSMIC core records at the level of disease classification.

## ACTIONABILITY RANK

Actionability rank is based on the availability of treatments for the combination of the variant, defined in Mutation Remark, and the Disease. It is not associated with individual trial records (rows in the download file), rather it is an indication of the most advanced development stage reached by any of the drugs that have been tested for the specified mutation-disease combination. Values range from approved, marketed drugs through clinical trial phases to case studies. There may be multiple drugs at each of the stages of drug development. Individual drugs are not assigned an Actionability rank, there is no intention to suggest a 'best' treatment.

There are four main ranked categories:

- 1/1†** - Approved marketed drug with demonstrated efficacy at the mutation. 1 indicates that the treatment is approved by the FDA. 1† indicates that the treatment is approved by a regulatory authority other than the FDA
- 2** - Phase 2 and 3 clinical results meet primary outcome measures\*
- 3** - Drug in ongoing clinical trials
- 4** - Case studies only

\*Primary outcome measure is met if the primary outcome (or any of the primary outcomes if there was more than one) has a p-value  $\leq 0.05$ , or the trial has been described as meeting objectives in publications, or for phase 1 trials, described as having no serious adverse event/toxicology issues.

There are two more categories:

- 6** - Use of the treatment depends on testing for another variant
- 7** - All trial results identified to date have not met their primary objectives

## PATIENT PRE-SCREENING

This value indicates whether the patients included in the trial were confirmed to have the variant/express the protein represented in the Mutation Remark column. Trials are included in Actionability either when confirmation of the variant/expression is a condition of recruitment, or when the trial details state the intention to correlate variant/expression with patient outcome.

There are five categories:

1. Yes - confirmation is part of the patient selection process
2. Expression - confirmation of protein expression
3. Overexpression - confirmed over expression
4. Comparison with wt - the aim of the trial is to compare outcomes in patients that do/do not have a variant
5. No - confirmation of the variant is not required for patient entry into the trial\*

\*Note that when Patient pre-screening category is 'No', trial results represent patients that have not undergone variant/expression screening. If at a later date results are published that correlate variant/expression with outcome, unselected patient results are replaced and the Patient pre-screening value is changed.

## GENE

Genes are represented using the [HGNC](#) gene symbol

## MUTATION REMARK

Identifies the gene, variant and specificity of patient selection/correlation with treatment efficacy. See Nomenclature of Variants for a full explanation. Filter this column to select specific variants.

## NOMENCLATURE OF VARIANTS (MUTATION SELECTIVITY)

Clinical Trials use variable levels of precision to describe and select patients with variants. This granularity is reflected in Actionability by variant selection categories. In order of decreasing precision the categories are:

- Single amino acid substitution
- Co-located mutations i.e. substitution of a protein residue by more than one alternative residues
- Cluster i.e. mutations at more than one location grouped by common functional consequence
- Exon i.e. any variant within a defined exon
- Gene where the location of the mutation is unspecified

There are five further categories:

1. Fusion: for gene fusions
2. Multigene: to indicate that patients have mutations identified in more than one gene
3. Set: where patients are grouped by the presence of variants in any of a list of genes
4. Region: any variant that affects a chromosomal region
5. Methylation: selection by level of DNA methylation

## HOW TO IDENTIFY THESE CATEGORIES IN THE DOWNLOAD FILE

The variant category can be identified by the nomenclature used for the Mutation Remark:

**Single amino acid substitutions:** Shown as the gene symbol followed by underscore followed by the unmutated residue in single letter code followed by the coordinate followed by the resulting residue in single letter code, e.g. AKT1\_E17K represents a variant of the gene AKT1 where the glutamate (E) at position 17 is substituted by lysine (K).

**Co-located substitutions:** Shown using the same nomenclature as single amino acid substitutions except that the letter representing the resulting residue is omitted. For example, ALK\_F1174 represents variants of ALK that result in the substitution of the phenylalanine residue at position 1174 with any of the substitutions that are possible.

**Clustered mutations:** Shown in two different ways:

1. A list of substitutions that are considered to be functionally equivalent, e.g. EGFR\_G719,L861Q,S768I (there are no spaces between the list items) represents variants in EGFR that lead to any substitution at G719 or the substitutions L816Q or S768I.
2. Used for insertions/deletions, shows the exon number followed by ins or del, e.g. EGFR\_Exon\_20ins represents EGFR exon 20 insertions.

**Exon level specificity:** Shown as the gene symbol followed by underscore followed by the word Exon followed by the exon number.

**Gene level specificity:** Where the variant can be anywhere in the protein coding sequence, is shown as the gene symbol followed by underscore followed by the word unspecified.

**Fusions:** Represented by the gene symbols connected by a hyphen, followed either by underscore followed by the word fusion, e.g. FGFR3-TACC3\_fusion. For fusions with defined subtypes, the subtype shown in parentheses, e.g. BCR-ABL e14a2 (b3a2). Sets of fusions, where only one partner is defined, are shown by the gene symbol of the defined partner followed by underscore followed by the plural word fusions, e.g. NTRK1\_fusions.

**Multi-gene patient selection:** Where the patient is required to have variants in two or more genes, are shown following the nomenclature described above connected by the word 'and'. Set selection: Where patients can have variants in any of a set of genes, are shown using the nomenclature described above connected by the word or.

**Chromosomal abnormalities:** Named using the chromosome number, arm and region, followed by, in parentheses, the symbols for genes that are suggested to be primarily connected with the functional consequence of the abnormality, if indicated in the trial description or literature.

**Methylation:** Represented by the gene symbol followed by underscore followed by the word methylation.

## DISEASE NAMES

The nomenclature used for Disease is a simplified version of the COSMIC classification system. COSO IDs, shown as Classification ID, allow linking Actionability records by specific disease to COSMIC core records.



## DRUG NAMES

Drug names used in Actionability give preference to the generic name, rather than commercial names. Early-stage compounds use a development name or code until a generic name becomes available, with preference given to the name used in the NCI Drug Dictionary, if available. Conceptually, Drug includes any therapy or treatment including those that are not traditionally considered as drugs, e.g. immunotherapies, cellular therapies and transplantation, radiotherapies. Surgical procedures are not included unless required to differentiate experimental and control arms of a trial.

## DRUG COMBINATIONS

The therapies used in clinical trials are very often combinations of drugs. When this is the case, the set of all drugs given to the patient is annotated and associated with the trial record. If the treatment is a single drug, the name is shown. If the treatment is a combination of more than one drug, a list of the names with intervening , is shown. For full details of the nomenclature used see Drug Names. The order of names does not imply the order that the treatments were given.

## TRIAL DETAILS

Clinical studies are annotated with information as available, including the source database identifier, the trial name, the development phase, the status of the trial, the primary (PCD) or estimated (ECD) completion date, patient treatment history, number of patients, and the stated primary outcome measure. For comparative trials (those with a control), additional annotations include the number of control patients and their treatment. If results of the trial are available, they are recorded. As trial results may be available in more than one form, e.g. in ClinicalTrials.gov and as a publication, preference is given to the most recent or complete set of results and the source of the data is indicated.

For most trials (exceptions explained below) the values of Number of Patients, Treated Number and Control Number indicate the total number of patients, the number receiving experimental treatment, and when relevant, the number receiving the control treatment, respectively. For single arm trials, the values of Number of Patients and Treated Number will be the same. For comparative

trials, Number of Patients is the sum of treated plus controls. Sometimes only the total number can be identified. For trials without results, any patient numbers are recruitment targets. Trials with results will show the number of patients included for calculation of the primary outcome.

Patient numbers are represented in a slightly different way for trials that compare patients with a variant to unmutated patients, and trials that compare patients by expression level or expression/absence of a marker.

Trials that compare patients with a variant to those that do not have the variant (mutant v wt) show Patient Pre-screening as 'Comparison with wt'. The value of Treated Number is the number of patients with the variant, the Control Number is the number of unmutated patients.

Trials that compare patients expressing a protein with those that don't, or compare patients with expression above/below a defined threshold, show Patient Pre-screening as 'Expressed/not'. The value of Treated Number is the number of patients with expression/expression above the threshold, Control Number is the number of patients not expressing/expressing below the threshold. When relevant the threshold value is shown in the Trial name field.

## TRIALS AND COHORTS

Clinical trials may have one or many subsets or cohorts. When results are released they may represent one, all, or some cohorts from a trial. Post-hoc segregation of patients into previously undescribed subgroups is common. Each row in the download file represents a trial cohort or subgroup. If a cohort has been assigned a name, it may be appended to/used in the absence of the Trial name. Trial cohorts that do not include patients with variants/expression, unless representing a control treatment, are not included in Actionability.

## **TRIAL PRIMARY COMPLETION DATE**

Primary Completion Date (PCD) is the date when all patient data required for calculation of primary outcome measures is expected to be/has been obtained. Completion Status is shown as Expected Completion Date (ECD) when the date is an estimate, PCD is shown when the date shown is the confirmed date of primary completion. Note that the trial is likely to continue beyond this date if there are multiple objectives.

## **PRIMARY OUTCOME MEASURE**

Clinical trials use a wide range of observational and statistical measures to represent patient outcome. Most trials specify a particular measure or measures that will be the key indicator of trial success or failure. This is usually referred to as the Primary outcome measure (PO). Trials may have more than one PO. Actionability uses a dictionary of primary outcome terms to record the primary outcome measure (see Primary Outcome Abbreviations).

## **DEVELOPMENT STATUS**

Drug development proceeds via a series of widely-recognised phases. Actionability uses an extended version of the FDA's phase definitions. Possible values are: Approved FDA, Approved other, Phase 3, Phase 2, Phase 1, Experimental, Orphan/Fast track, Case study, Out of trials human study, Retrospective/Meta-analysis, Phase 4, Unknown.

## **TRIAL STATUS**

Trial status indicates the progress of the trial. Not all trials specify status and many trials do not report at every stage. Possible values are: Not yet recruiting, Recruiting, Active, Complete, Terminated, Suspended, Withdrawn, Unknown. Definitions of these stages can be found at [ClinicalTrials.gov](https://clinicaltrials.gov)

## **RESULTS AVAILABILITY**

Indicates whether the trial/cohort has results or not. Note that if the value in Patient pre-screening is No, results do not reflect variant/expression status.

## RESULTS MEASURES

As they become available, the results of trials are recorded. Clinical trials use a wide range of outcome measures. All time measurements are represented in months and as mean values with 95% Confidence Intervals. The most used measures are recorded in the following columns:

Objective response rate - treatment

Objective response rate - control

Objective response rate - 95% confidence interval

Objective response rate - p-value

Overall survival - treatment

Overall survival - control

Overall survival - hazard ratio

Overall survival - 95% confidence interval

Overall survival - p-value

Progression free survival - treatment

Progression free survival - control

Progression free survival - hazard ratio

Progression free survival - 95% confidence interval

Progression free survival - p-value

Time to progression - treatment

Time to progression - control

Time to progression - hazard ratio

Time to progression - 95% confidence interval

Time to progression - p-value

Disease control rate - treatment

Disease control rate - control

Disease control rate - p-value

Duration of response - treatment

Duration of response - control

Duration of response - 95% confidence interval

Duration of response - p-value

Number of patients with complete response

Number of patients with partial response

Number of patients with stable disease

Regression free survival - treatment

Regression free survival - control

Regression free survival - hazard ratio

Regression free survival - 95% confidence interval

Regression free survival - p-value

Three additional measures specific to haematological disorders are captured:

1. Blood response – Defines the measure using one of the following controlled vocabulary terms: Complete cytogenetic; Complete haematologic; Complete molecular; Major cytogenetic; Major haematologic; Major molecular; Partial cytogenetic; Complete morphologic
2. Response value – percentage of patients
3. Timepoint – time after treatment that measurement was taken

Other results measures are recorded in the column Progression Remark.

Note that results from studies comparing the effect of treatment in patients with/without a variant (with a Patient pre-screening value of 'Comparison with wt') or with high/low expression (with a Patient pre-screening value of 'Expressed/not') record results for mutated/expressing patients in results columns used for treatment values and results for unmutated/non-expressing patients in results columns used for control treatment values.

## PROGRESSION REMARK

Controlled vocabulary remarks with five subtypes. More than one subtype may be shown, multiple comments are separated by commas.

1. Results for less common primary outcomes that are not recorded in a defined result column. The primary outcome measure type is indicated by an abbreviation. The abbreviations used are shown in the table Primary Outcome Abbreviations
2. Indication that a publication suggests the trial has/has not met its primary objective. If described to have met the primary objective, the remark is 'Primary outcome met'. If described to have not met the primary objective, the remark is 'Primary outcome not met'.
3. For trials that have a Trial Status of Terminated or Withdrawn, describes why the trial ended, if identified, e.g. Slow accrual, Toxicity issues, Lack of efficacy.
4. Publication comments on treatment efficacy or correlation of variant/expression with efficacy, e.g. No benefit of treatment, Response correlated with mutation status, Response not correlated with expression status.
5. For Phase 1 studies, indicates the incidence of serious adverse events, if identified, with the abbreviation SAE followed by a percentage of patients.

## TESTING REQUIRED

This annotation indicates whether patients must be tested to confirm the presence of the indicated mutation before they can receive the indicated treatment. It is applied only for drugs that have regulatory approval. Possible values are: Required, Not required, Expression, wt KRAS, EGFR expression and KRAS mutation, HER2 expression.

## TREATMENT HISTORY

Indicate whether the patients have/have not received prior treatment for the indicated disease. There are three categories:

1. Untreated
2. Previously-treated
3. Blank meaning either a mixture, or not specified

## PATIENT AGE

Indicates trials that select paediatric or geriatric patients. Note this does not represent a specific age range.

## LAST UPDATED

Indicates when details of a trial record were last edited, allowing the identification of records that have new details. The date is updated when any of the following details of the trial are changed: Name, ID, Treatment history, Primary completion status, Primary completion date, Patient count, Control patient count, Primary outcome type, Progression remark, Development stage, Trial status, Disease type, Treatment, Results availability, Evidence source, or any of the results details.

## PRIMARY OUTCOME ABBREVIATIONS

DESCRIPTION	ABBREVIATION
12 Month treatment free remission	TFR12
2-HG suppression	2HG
Absorption rate	Cmax/AUC
Accrual rate	AR
Acute leukemia response-complete rate	ALRC
Adverse Events of Primary Interest	AEPI
Altered genomic signature	GenS
Best overall response	BOR
Biomarker discovery	BD
Biomarker protein downregulation	BD
Bone scan response rate	BSR
Brain metastasis response rate	BMRR
Breast-Conserving Surgery Rate	BCSC
Cardiac event	CE
Cell cycle arrest	CCA
CelTIL score	CS
Change in CD3+ lymphocytes	CD3+
Change in Ki-67 expression	Ki67
Change in Cortisol level	CORT
Change in ocular side effect management	OSE
Circulating tumour cells	CTC
Clearance of ctDNA	CTDNA

DESCRIPTION	ABBREVIATION
Clinical activity	CA
CNS ORR, Intracranial ORR	IORR
Complete cytogenetic response	CCyR
Complete haematologic response	CHR
Complete metabolic response	CMR
Complete molecular response	CMR
Complete morphologic response	CMR
Complete remission	CRM
Complete response, Pathological complete response	CR
Composite complete remission	cCR
Cost of therapy	CO
CR, DFS	CR, DFS
CR, DFS, OS	CR, DFS, OS
CR, EFS	CR, EFS
CR, EFS, OS	CR, EFS, OS
CR, MpaR	CR, MpaR
CR, ORR	CR, ORR
CR, OS	CR, OS
CR, PFS	CR, PFS
CRM, PFS	CRM, PFS
ctDNA clearance	ctDNA
ctDNA mutation detection	CTM
Cumulative incidence of relapse	CIR
Cytogenetic response	CyR
Cytokine release syndrome rate	CRS
DCR, ORR	DCR, ORR
DCR, ORR, DOR	DCR, ORR
DCR, TTP	DCR, TTP
DFS, OS	DFS, OS
Disease control rate, Clinical benefit rate	DCR
Disease free survival, relapse free survival, regression free survival, recurrence free survival	RFS
Distant Brain Metastasis-free Survival	DBMFS
Distant metastasis free survival	DMFS
Donor engraftment, GVHD rate	DE
Drug resistance	DR
Duration of response	DOR
Early tumour shrinkage	ETS
EFS, OS, ORR	EFS, OS, ORR



DESCRIPTION	ABBREVIATION
EFS, pCR	EFS, pCR
Endocrine Sensitive Disease Rate	ESDR
Erythroid response	ER
Estradiol blood concentration	EBC
Event free survival	EFS
Excellent and Indeterminate Response - defined by ATA 2015	E&IR
Failure free survival, Time to treatment failure	FFS
FFS, DOR, PFS	FFS, DOR, PFS
FLT uptake	FLT
Functional airway response	FAR
Globulin level	GL
Grade 1-2 Cytokine Release Syndrome	Grade I-II CRS
Grade 4 Cytokine Release Syndrome	Grade III CRS
Haematological response	HR
Hyperglycemia	HYG
ICANS, CRS	ICANS, CRS
Immune cell infiltration	ICI
Immune effector cell associated neurotoxicity syndrome rate	ICANS
Immune response	IR
Improved hearing	IH
Intracranial disease control rate	IDCR
Intracranial duration of response	IDOR
Intracranial progression free survival	IPFS
Intracranial Response Rate	IRR
Intracranial time to progression	ITTP
Intratumoural hormone level	IHL
Invasive Breast Cancer-Free Survival	IBCFS
IPFS, IORR	IPFS, IORR
IPFS, IORR, IDCR	IPFS, IORR, IDCR
IRR, IPFS	IRR, IPFS
Laryngectomy-free survival	LFS
Leukemia free survival	LFS
Locoregional control	LRC
Lymph node clearance rate	LNCR
Major cytogenetic response	MCyR
Major haematologic response	MHR
Major molecular response	MMR
Major pathologic response	MpaR
Malonyl carnitine and tripalmitin levels	MCT

DESCRIPTION	ABBREVIATION
Marker correlation with progression	MkP
Marker phosphorylation	MP
Maximum tolerated dose/toxicity	MTD
Metabolic endpoints (malonyl carnitine and tripalmitin levels)	ME
Metabolic response	MetR
Minimal residual disease (MRD)	MRD
Molecular response	MR
MTD, ORR, Toxicity	MTD, ORR, Tox
MTD, OS	MTD, OS
Neutropenia	NP
Neutrophil recovery	NR
No CNS progression	CNSN
Non-relapse mortality	NRM
Not defined	ND
Number of adverse events	nAE
Organ preservation	OP
ORR, DOR	ORR, DOR
ORR, EFS	ORR, EFS
ORR, OS	ORR, OS
ORR, PFS, DOR	ORR, PFS, DOR
ORR, PFS, OS	ORR, PFS, OS
ORR, TTP, PFS	ORR, TTP, PFS
OS, EFS	OS, EFS
OS, ORR, DOR	OS, ORR, DOR
OS, PFS	OS, PFS
Ovarian cyst incidence	OC
Overall Response Rate	ORR
Overall survival	OS
PAM50 proliferation signature	PAM50
Participants with $\leq 1\%$ BCR-ABL1 at 12m	MMR1PC
Pathologic Response	PaR
PFS, DCR	PFS, DCR
PFS, DOR	PFS, DOR
PFS, MTD	PFS, MTD
PFS, ORR	PFS, ORR
PFS, OS, DOR	PFS, OS, DOR
PFS, RFS	PFS, RFS
PFS, TTP	PFS, TTP

DESCRIPTION	ABBREVIATION
PFS, TTP, OS	PFS, TTP, OS
Pre-operative Endocrine Prognostic Index (PEPI score)	PEPI
Progression free survival	PFS
Prostate Specific Antigen (PSA) response rate	PSA
PSA, ORR	PSA, ORR
Quality of life	QOL
Radiographic response rate	RRR
Radiologic complete response	RCR
Radiologic partial response	RPR
Rate of Diarrhoea	RD
Recruitment	REC
Reduced allele burden	RAB
Reduced target expression level	IHC level
Reduction $\geq 1$ log or undetectable BCR-ABL	BCR-ABL-
Reduction of BCR-ABL1 stem cells	BASC
Resection rate	RR
Residual Cancer Burden I	RCB1
Residual Cancer Burden II	RCB2
Residual disease, Residual cancer burden	MRD
Response rate	RR
RFS, EFS	RFS, EFS
Spleen volume reduction	SVR
Target-specific T cell activity	TCA
Time to next treatment	TTN
Time to progression	TTP
Time to response	TTR
Time to Second Objective Disease Progression	PD2
Total Mesorectal Excision Free Survival Rate	TMEFSR
Total symptom score	TSS
Transplant-ready patient rate	TR
Treatment discontinuation	TD
Treatment rate, Treatment completion, Compliance, Adherence to protocol	TR
TTP, ORR	TTP, ORR
TTP, OS	TTP, OS
Tumour Burden	TB
Tumour microenvironment changes	TMC
Tumour volume	TV
Unknown	UN

DESCRIPTION	ABBREVIATION
Vector copy number	VCN
Vitamin C serum bioavailability	VCB

### FURTHER INFORMATION

Since Actionability v7 this product is freely available for non-commercial use. Please make sure you read and understand whether you count as commercial or non-commercial via our licensing page (<https://cancer.sanger.ac.uk/cosmic/license>)

If you are using COSMIC Actionability for non-commercial purposes, you can register for an account and download the data directly from COSMIC (<https://cancer.sanger.ac.uk/cosmic/download>)

To access COSMIC Actionability for commercial use, please contact our Sales Partner QIAGEN ([bioinformaticssales@qiagen.com](mailto:bioinformaticssales@qiagen.com))