Supplementary Table S1. Gene lists for NGS Version 1 and 2. Refseq: Reference of the transcript in the NCBI database used for NGS sequencing.

Gene	RefSeq	Exons	Gene	RefSeq	Exons	Gene	RefSeq	Exons
ABL1	NM_007313	1 to 11	*FGFR3*	NM_000142	2 to 19	*PTCH1*	NM_001083603	1 to 28
AKT1	NM_005163	4	*FGFR4*	NM_002011	2 to 18	*PTEN*	NM_000314	1 to 9
AKT2	NM_001626	2 to 14	*GNAQ*	NM_002072	5	*RB1*	NM_000321	1 to 27
ALK	NM_004304	1 to 29	*HRAS*	NM_005343	2 to 4	*RET*	NM_020975	1to 20
APC	NM_001127511	1 to 15	*IGF1R*	NM_000875	1 to 4	*ROR1*	NM_005012	1 to 9
AXL	NM_021913	1 to 20	*JAK2*	NM_004972	1to 25	*ROR2*	NM_004560	1to 9
BRAF	NM_004333	15	*JAK3*	NM_000215	2 to 24	*ROS1*	NM_002944	1 to 43
BRCA1	NM_007294	2 to 24	*KDR*	NM_002253	1 to 30	*RYK*	NM_002958	1 to 15
BRCA2	NM_000059	2 to 27	*KIT*	NM_000222	1 to 21	*SDHAF2*	NM_017841	1 to 43
RAF1	NM_002880	1 to 17	*KRAS*	NM_004985	2 et 3	*SDHB*	NM_003000	1 to 8
CDKN2A	NM_000077	1 to 3	*MERTK*	NM_006343	1 to 19	*SDHC*	NM_001035511	1 to 5
CSF1	NM_172212	1 to 9	*MET*	NM_001127500	2 to 21	*SDHD*	NM_003002	1 to 43
CSF1R	NM_005211	2 to 22	*MPL*	NM_005373	1 to 12	*SMARCB1*	NM_003073	1 to 9
DDB2	NM_000107	1 to 10	*MST1R*	NM_001244937	1 to 19	*SMO*	NM_005631	1 to 12
DDR1	NM_001202523	3 to 21	*MTOR*	NM_004958	1 to 58	*SRC*	NM_005417	4 to 14
DDR2	NM_006182	4 to 19	*MUSK*	NM_001166280	1 to 16	*STK11*	NM_000455	1 to 10
EGFR	NM_005228	19 to 21	*NRAS*	NM_002524	2 to 4	*TEK*	NM_000459	1 to 23
ERBB2	NM_004448	1 to 27	*PDGFA*	NM_033023	1 to 17	*TIE1*	NM_005424	1 to 23
FLT1	NM_002019	1 to 32	*PDGFB*	NM_002608	1 to 8	*TP53*	NM_000546	2 to 12
FLT3	NM_004119	1 to 24	*PDGFRA*	NM_006206	2 to 23	*TSC1*	NM_001162427	3 to 23
FLT4	NM_182925	1 to 30	*PDGFRB*	NM_002609	2to 23	*TSC2*	NM_000548	2 to 42
FGFR1	NM_023106	4 to 21	*PIK3CA*	NM_006218	10 et	*TYRO3*	NM_006293	1 to 10
FGFR2	NM_000141	2 to 27	*PIK3R1*	NM_181523	2 to 16	*VHL*	NM_000551	1 to 9

Genes added in Panel V2 (October 2014)

For most of these genes (61/69), the coding areas were sequenced to 250*average depth and achieved a 90% breadth of coverage at a minimum depth of 50 reads. The sequencing was focused on the hotspot regions of targetable or clinically relevant mutations for the remaining eight genes.

Supplementary information S2. Characterization procedures and classification of molecular alterations.

The size distribution of the DNA amplicons was analyzed on the 2200 TapeStation (Agilent Technologies, Santa Clara, USA) using the High Sensitivity DNA Reagent Kit (Agilent Technologies Santa Clara, USA). Template preparation, emulsion PCR, and Ion Sphere Particle (ISP) enrichment were performed using the Ion OneTouchTM 2 kit (Thermo Fisher Scientific, Waltham, Massachusetts, USA) according to manufacturer's instructions. The ISPs were loaded onto an Ion 318TM Chip Kit V2 (Thermo Fisher Scientific, Waltham, Massachusetts, USA) and sequenced using an Ion PGMTM Sequencing 200 Kit V2 (Thermo Fisher Scientific, Waltham, Massachusetts, USA) on the Ion Torrent PGMTM for 500 cycles.

The pipeline includes quality score assignment, alignment to the human genome 19 reference, mapping quality QC, coverage analysis, and variant calling. After completion of the primary data analysis, lists of detected sequence variants (Single nucleotide variants [SNVs] and INDELs) were compiled in the Variant Call Format (VCF) files. For downstream analysis, variants with minimum coverage of 50 reads containing at least 10 mutant reads were selected. Variant calls were further analyzed using variant filtering and annotation using COSMIC v.64 released on 2013, March 26th[online version only [20]] and dbSNP build 135, released on 2012, June 6th.[online version only [21]] The variants were filtered according to their frequency (>5% for SNVs and >10% for INDELs), strand ratio (>0.2), and reads coverage (>50X for SNVs and 100X for INDELs).

We used the knowledge database of somatic mutations Cosmic v.64 released on 2013, March 26th, to classify each selected variant as **'**pathogenic**'**, **'**unknown pathogenicity**'**, or **'**probable pathogenicity**'** variants. Oncogenes with known activating mutations and amplifications (gene copy number ≥6) prevailed. Well characterized hot-spot mutations such as *PI3KCA* mutations (E542K, E545K/Q, H1047L/R) were selected for treatment recommendation. Homozygous deletion or bi-allelic inactivation (inactivating mutation and/or heterozygous deletion) for tumor suppressor genes (such as *PTEN*) were then taken into account. Passenger mutations or mutations known to be related to treatment resistance (for instance *KRAS*) were taken into account only in respect of specific tumor types Gene gains or heterozygous deletions were not considered.

The MTB defined a MBRT on the basis of the availability of drugs hitting either directly the selected target protein or the pathway activated by the altered protein.