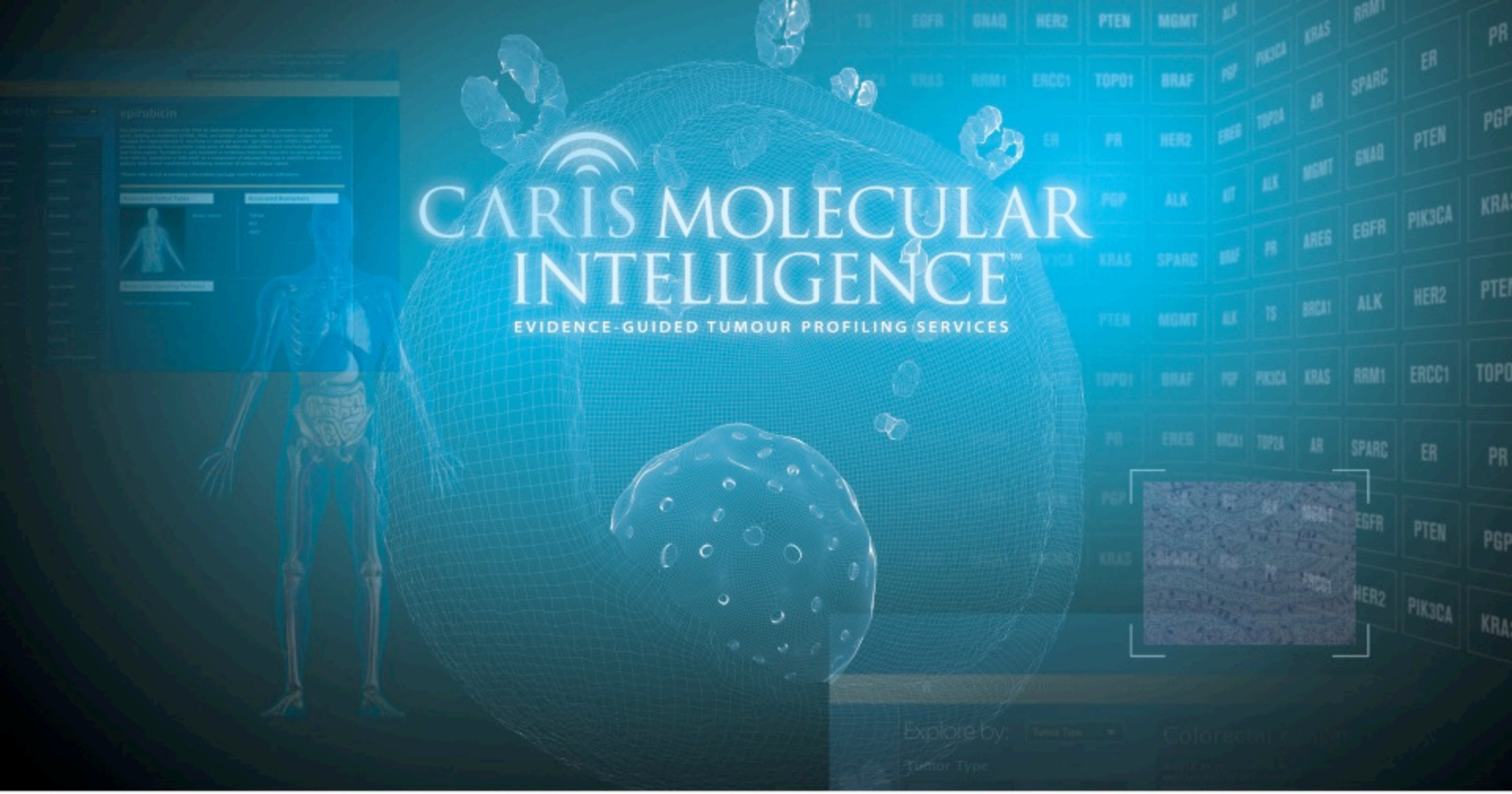


Caris Life Sciences®
Molecular Intelligence™ Service

CARIS LIFE SCIENCES

EA114EE 09/15/14

Caris Life Sciences

Fulfilling the promise of precision medicine

Leading biosciences company focused on improvement of cancer care through delivering innovative diagnostic and theranostic services

- Founded 2008 in US, located in Dallas and Phoenix
- Since 2012 offering services throughout Europe and many international markets

Fielding a powerful team of professionals

managing laboratory performance and evidence processes, including

- medical oncologists
- pathologists
- molecular geneticists
- research scientists

Unmatched Laboratory Quality

6,000 square meter, Phoenix-based laboratory

- Licensed and validated according to ISO 15189:2012, CLIA and CAP standards, CE mark validation
- every patient's results are personally reviewed by a qualified molecular pathologist and geneticist before being released.

Caris Molecular Intelligence ™ provides actionable treatment options – supported by the strongest clinical evidence

Thorough and Accurate Biomarker Analysis of a Patient's Tumour

Correlates Biomarker Targets to Therapeutic Agents

Extensive Clinical Literature Assessment

Informs Treatment Decisions Through an Actionable Report

Actionable Biomarkers Found in 95% of Cases

Average of 25 Clinically Relevant Results Reported per Patient

Caris Molecular Intelligence May Be Clinically Helpful For

Metastatic cancers refractory to standard treatments, e.g.

- Breast cancer
- Lung cancer
- Ovarian cancer
- Colorectal cancer

Aggressive cancers with few standard treatment options, e.g.

- Melanoma
- Pancreatic cancer

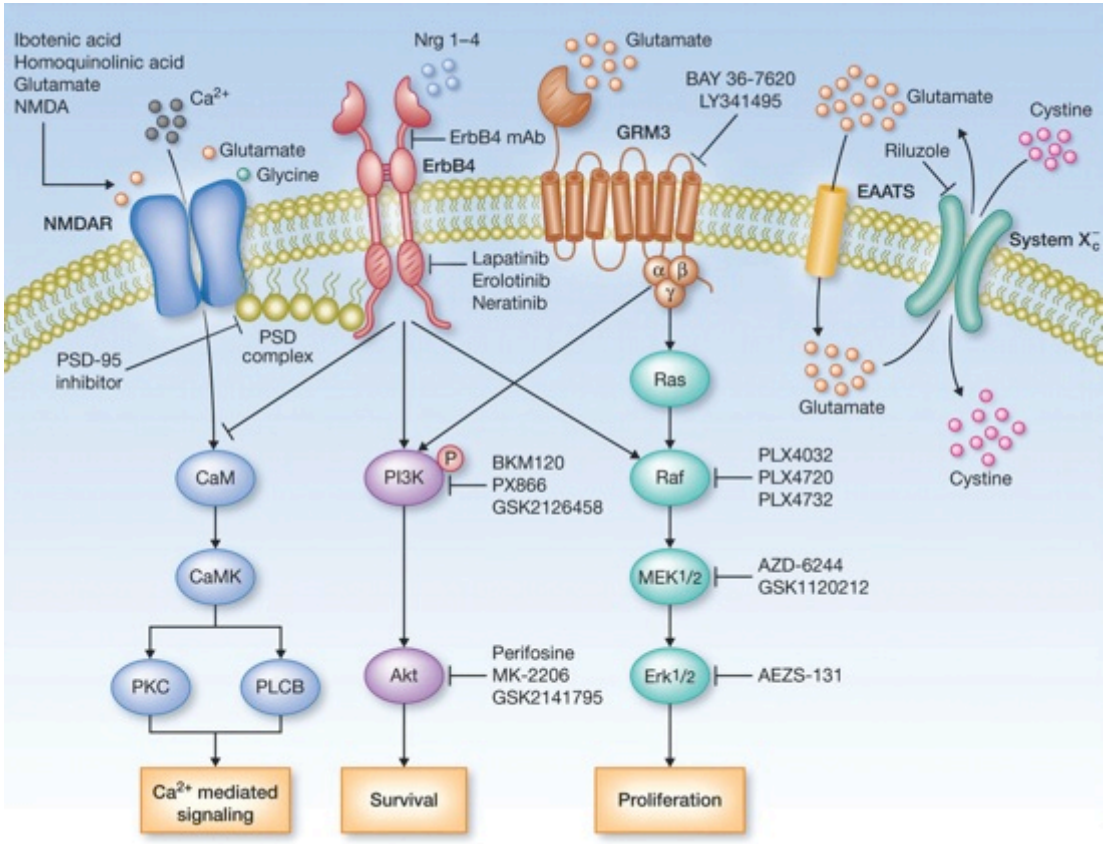
Rare and less common cancers with limited standard of care options, e.g.

- Sarcomas
- Gliomas
- Cancer of Unknown Primary (CUP)

Relevant Biomarkers are Analysed Using and Proven Accepted Technologies

BIOLOGIC PROCESS	TECHNOLOGY	BIOMARKERS
DNA Mutations	**Next Generation Sequencing**	ABL1, AKT1, ALK, APC, ATM, BRCA1/2, BRAF, CDH1,cKIT, cMET, CSF1R, CTNNB1, EGFR, ERBB2 (HER2), ERBB4, FBXW7, FGFR1, FGFR2, FLT3, GNA11, GNAQ, GNAS, HNF1a, HRAS, IDH1, JAK2, JAK3, KDR (VEGFR2), KRAS, MPL, NOTCH1, NPM1, NRAS, PDGFRα, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARCB1, SMO, STK11, TP53, VHL
	PCR	BRAF
	Sanger Sequencing	IDH2
DNA, RNA	**Fragment Analysis**	EGFRvIII, MSI
Gene Rearrangements Gene Copy Number Variations	**FISH / CISH**	ALK, cMET, EGFR, HER2,, ROS1, TOP2A, 1p19q
Epigenetic Changes	**Pyro-sequencing**	MGMT Methylation
Protein Expression	**IHC**	AR, cMET, EGFR , ER, ERCC1, HER2, H3K36me3, MLH1, MSH 2,6, MGMT, PBRM1, PD-1, PD-L1, Pgp, PMS2, PR, PTEN, RRM1, SPARCm, SPARCp, TLE3, TOPO1,TOP2A, TS, TUBB3

Caris has established over 33,000 biomarker rules to help guide treatment decisions

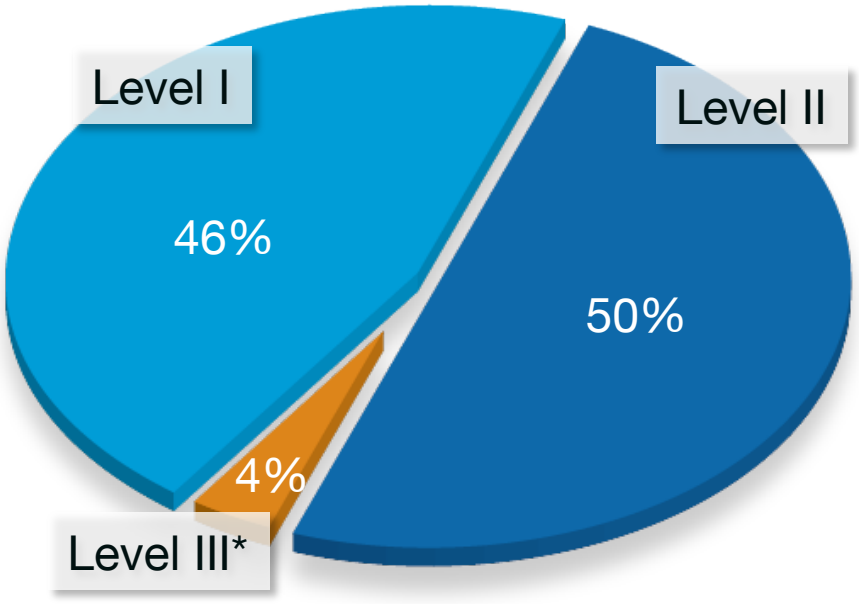


The Caris "Rules Engine" evaluates biomarker and drug associations along each molecular pathway.

The evidence team continually updates the rules to resolve competing or conflicting biomarker interactions

The Caris processes make sure we identify the drugs offering the most – and the least – potential clinical benefit for CANCER patients.

96% of drug / biomarker associations are based on Level I or Level II evidence



Current Methods of the U.S. Preventive Services Task Force

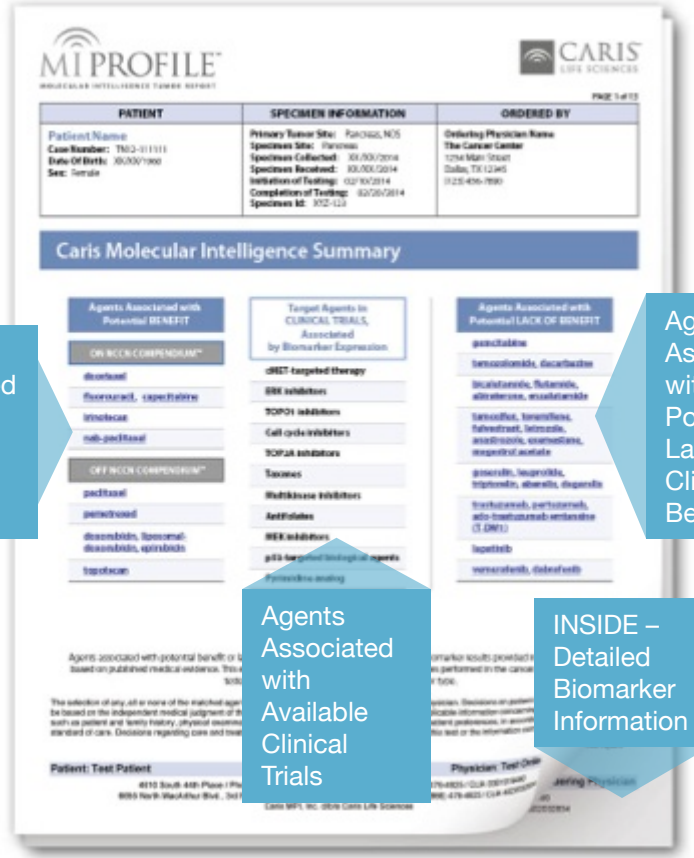
As Applied by Caris Life Sciences

Hierarchy of Research Design

I	Evidence obtained from at least one properly randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies and case reports, or reports of expert committees.

* Level III evidence associates ROS1 to crizotinib, which is included in the NCCN Guidelines for the treatment of NSCLC

Clinical Utility Maximised with Easy-To-Interpret Reports



Average of 25 Clinically Relevant Results Reported per Patient.*

Actionable Biomarkers Found in ~95% of Cases.

Top page:

- Easy-to-Interpret Summary

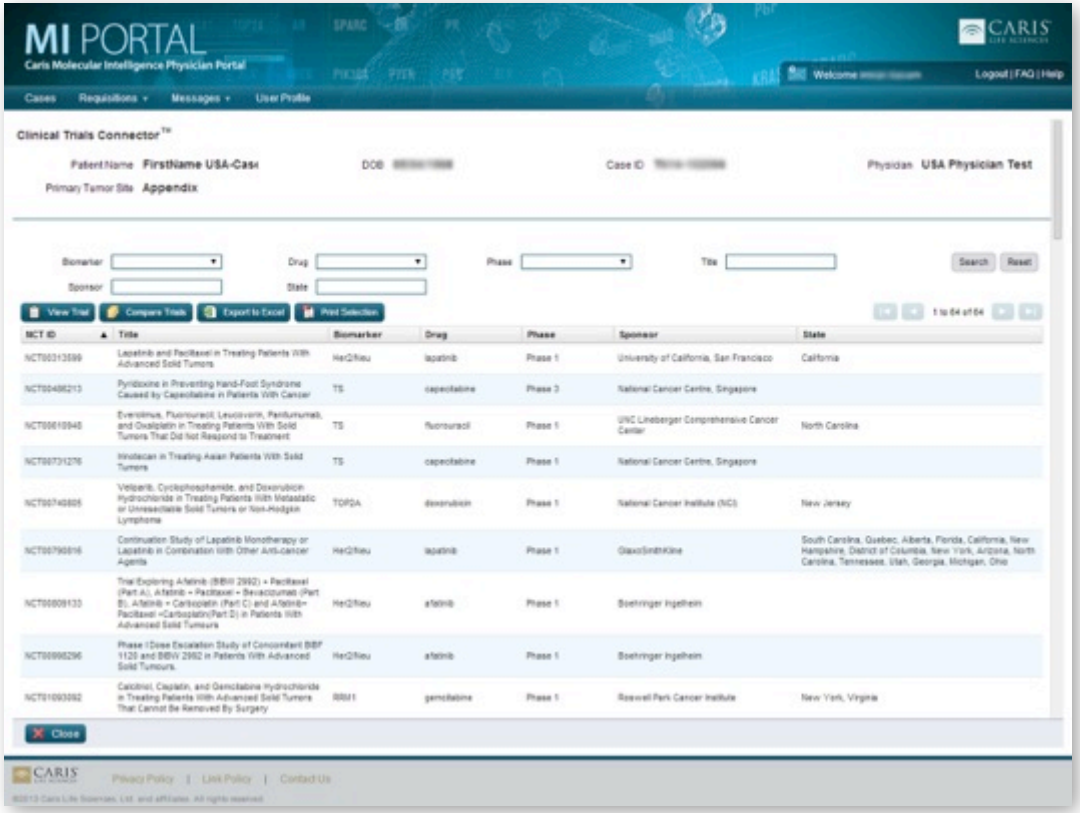
Content:

- Detailed Biomarkers Results
- Clinical Trial Information
- References Supporting Biomarker Drug Associations

➪ Caris Offers Consultation to Support Interpretation of the Reports

* MI Profile offering. Clinically relevant results include agents with potential benefit, agents with lack of potential benefit and clinical trials.

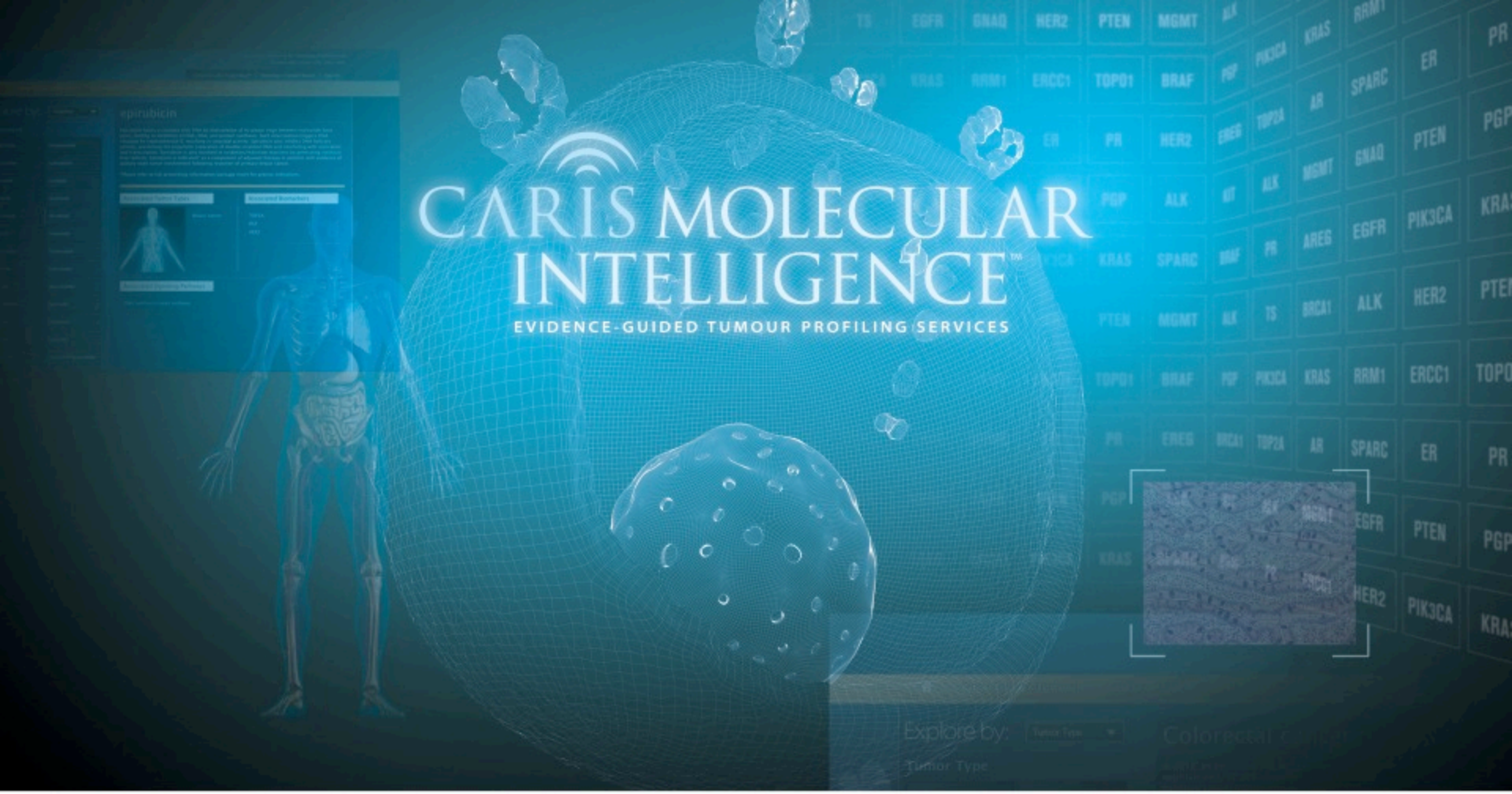
Connecting Patients to Relevant Clinical Trials



The **Clinical Trials Connector** examines thousands of open and enrolling clinical trials

Matches clinical trials based on:
- Biomarker profile
- Tumour type
- Gender
- Age (date-of-birth)

The Clinical Trials Connector™ simplifies the process of finding the right trial for cancer patients



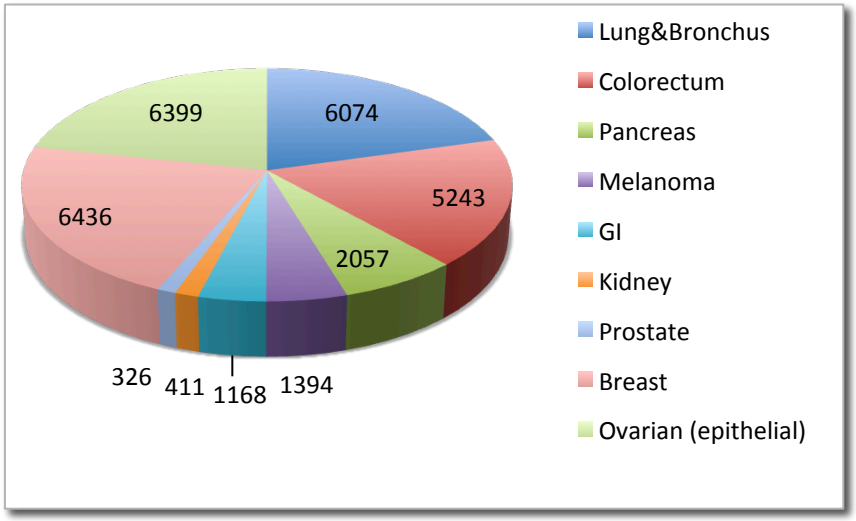
Summary of Published and Presented Evidence, Evaluating the Clinical Utility of CMI, in Clinical Studies and Clinical Practice

(updated May 2014)

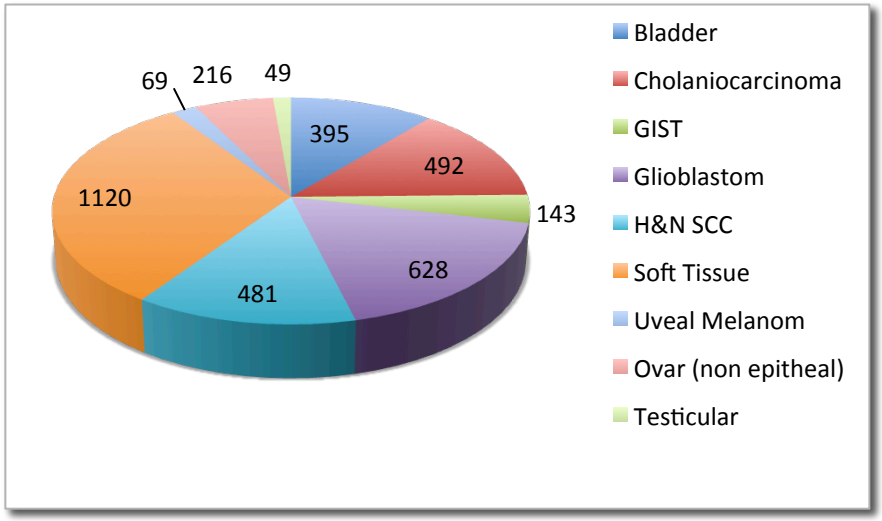
CARIS® LIFE SCIENCES

Caris has profiled more than 60,000 patients worldwide[1]

Most Common Cancers[2,3]



Less Common Cancers [2,3]



The complete Caris database covers biomarker profiles of over 150 histological cancer subtypes.

Caris Molecular Intelligence is most suitable for

- **Metastatic cancers** refractory to standard treatment e.g. Breast, Lung, Colorectal, Ovarian cancer
- **Rare and less common cancers** with limited standard options e.g. Sarcoma, Glioma, CUP
- **Aggressive cancers** with few standard options e.g. Melanoma, Pancreatic cancer

1) Russell et al 2014 2) Gatalica 2013 3) Von Hoff ASCO 2013

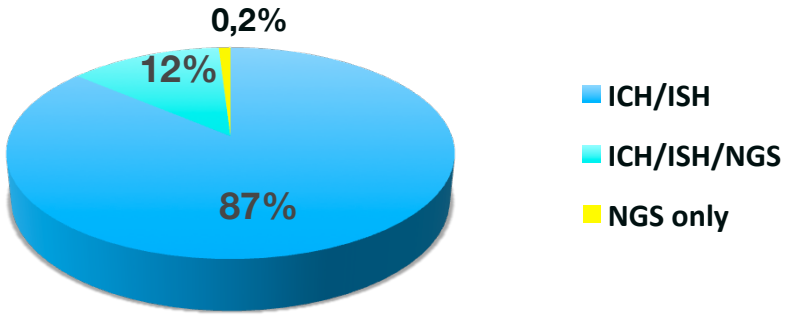
Identifies druggable targets in 90-100% of patients profiled using a multi-technology platform

Biomarker-drug associations identified in 12.265 patients profiled[16]:

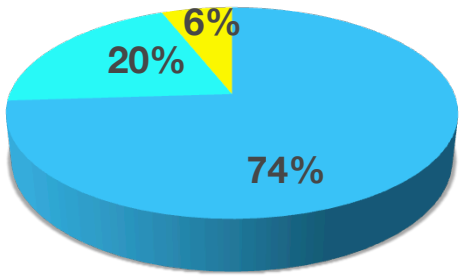
Drugs with potential benefit	Drugs with potential lack of benefit
in **93%** of reports	in **97%** of reports

Utilising a multi-technology platform is crucial for delivering this rate of biomarker–drug associations (displayed as percent of reports):

Agents associated with potential benefit



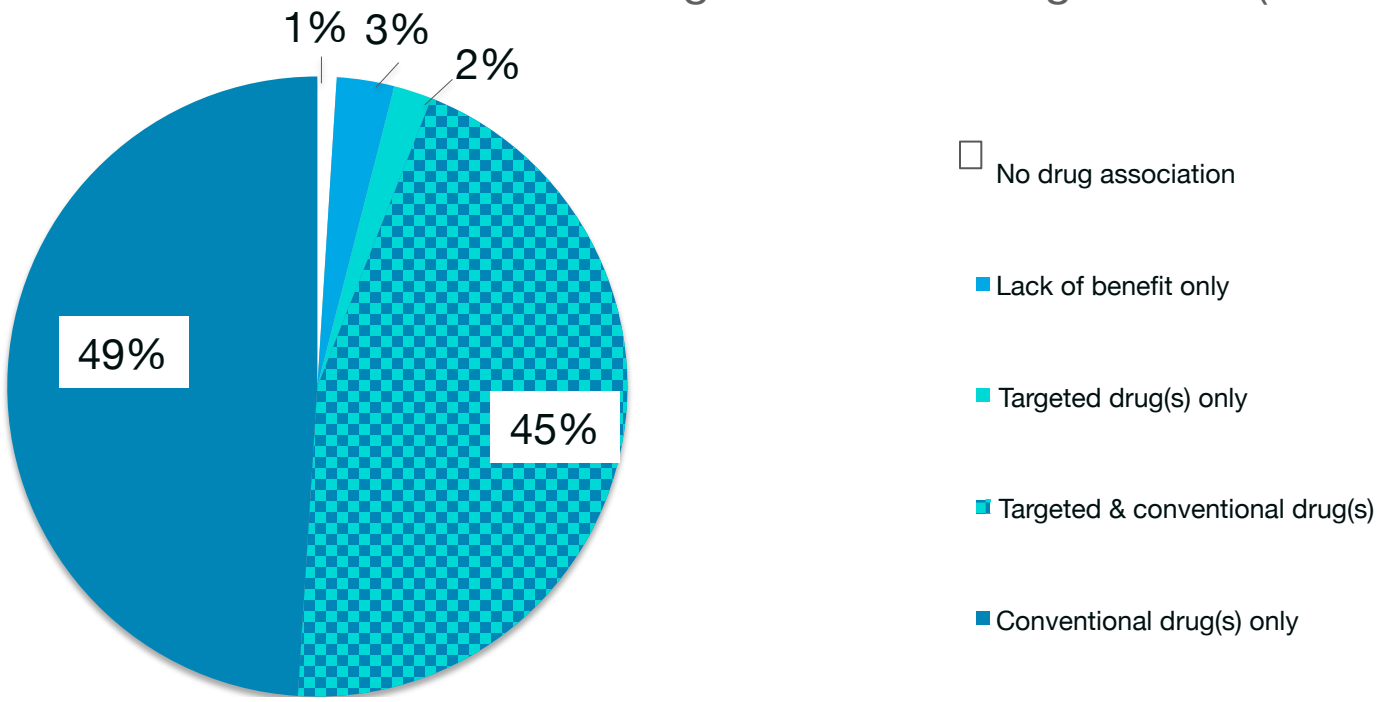
Agents associated with potential lack of benefit



16) Caris data on file

Reports associations to conventional and targeted therapies

Example: Treatment Associations using Tumour Profiling of CUP (n=1'459)[5, 8b]

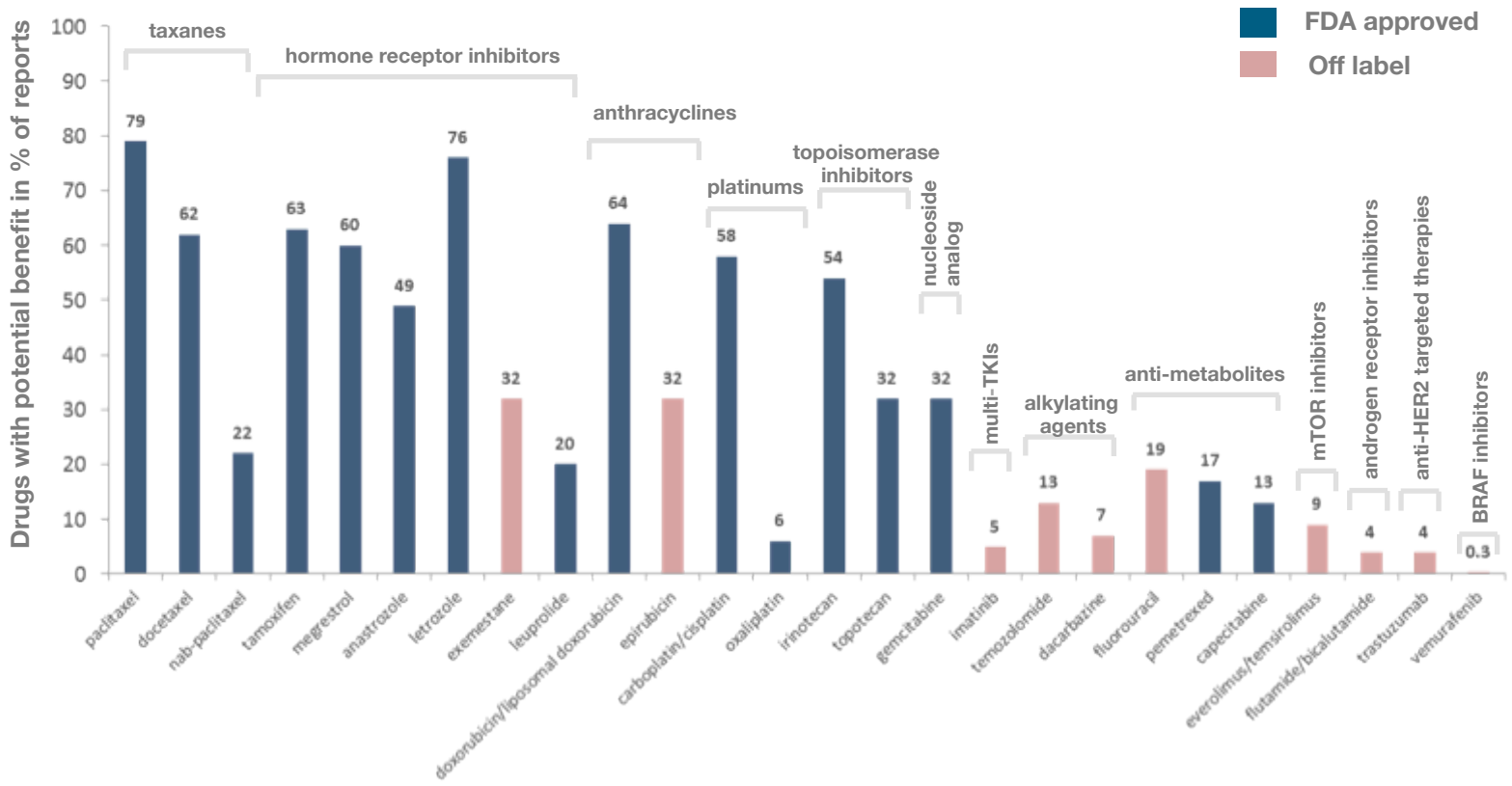


Targeted drugs include TKIs, mAbs, anti-steroidals, mTOR inhibitors
Conventional drugs include alkylating agents, anthracyclines, camptothecans, pyramidine antagonists, antimetabolites, taxanes, etc.

5) Gatalica Z, EJC 2013 8b) Caris data on file

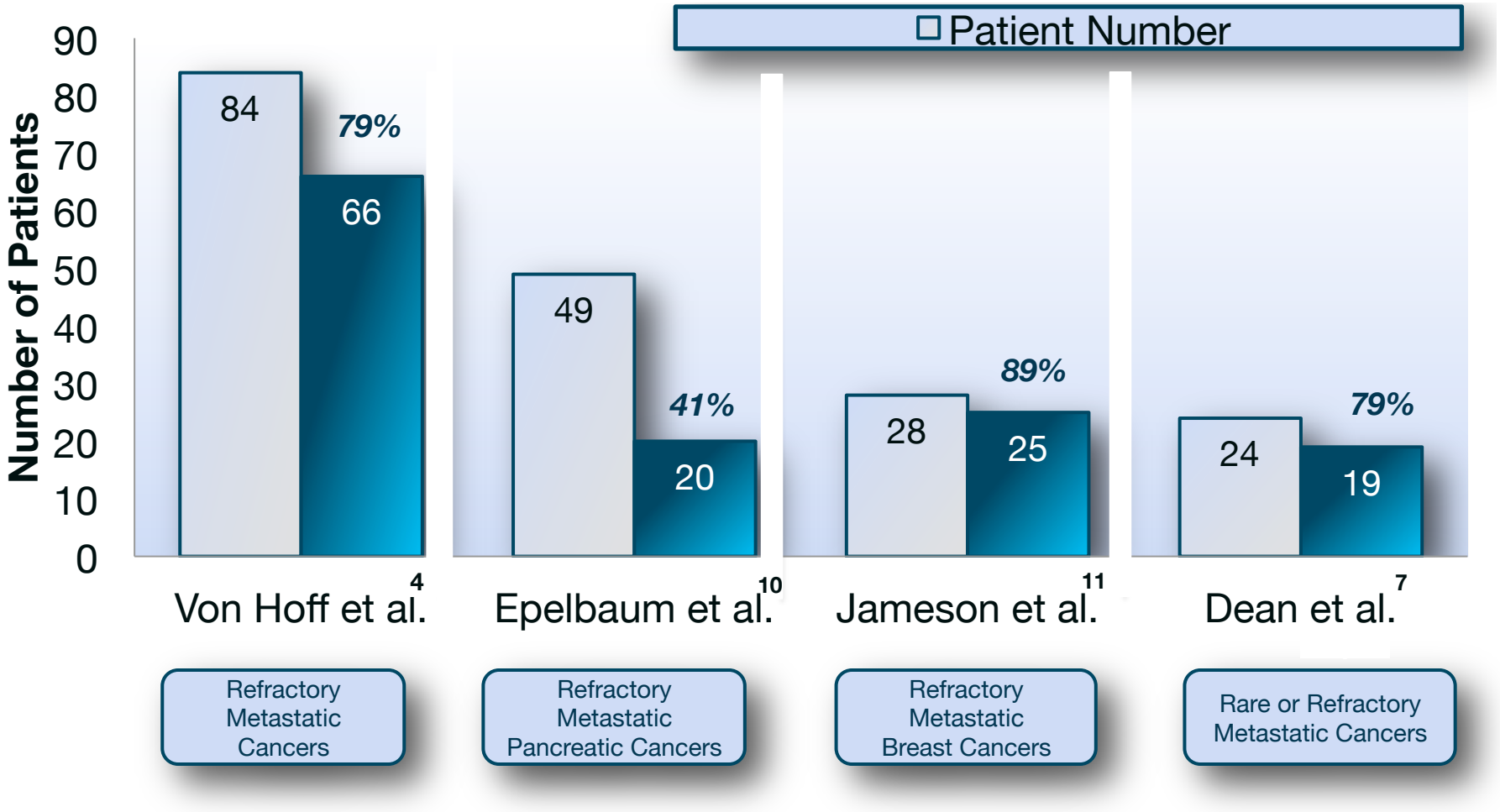
Reports associations to conventional and targeted therapies

Example 2: Treatments with potential benefit, ovarian cancer registry (n= 348)[17]

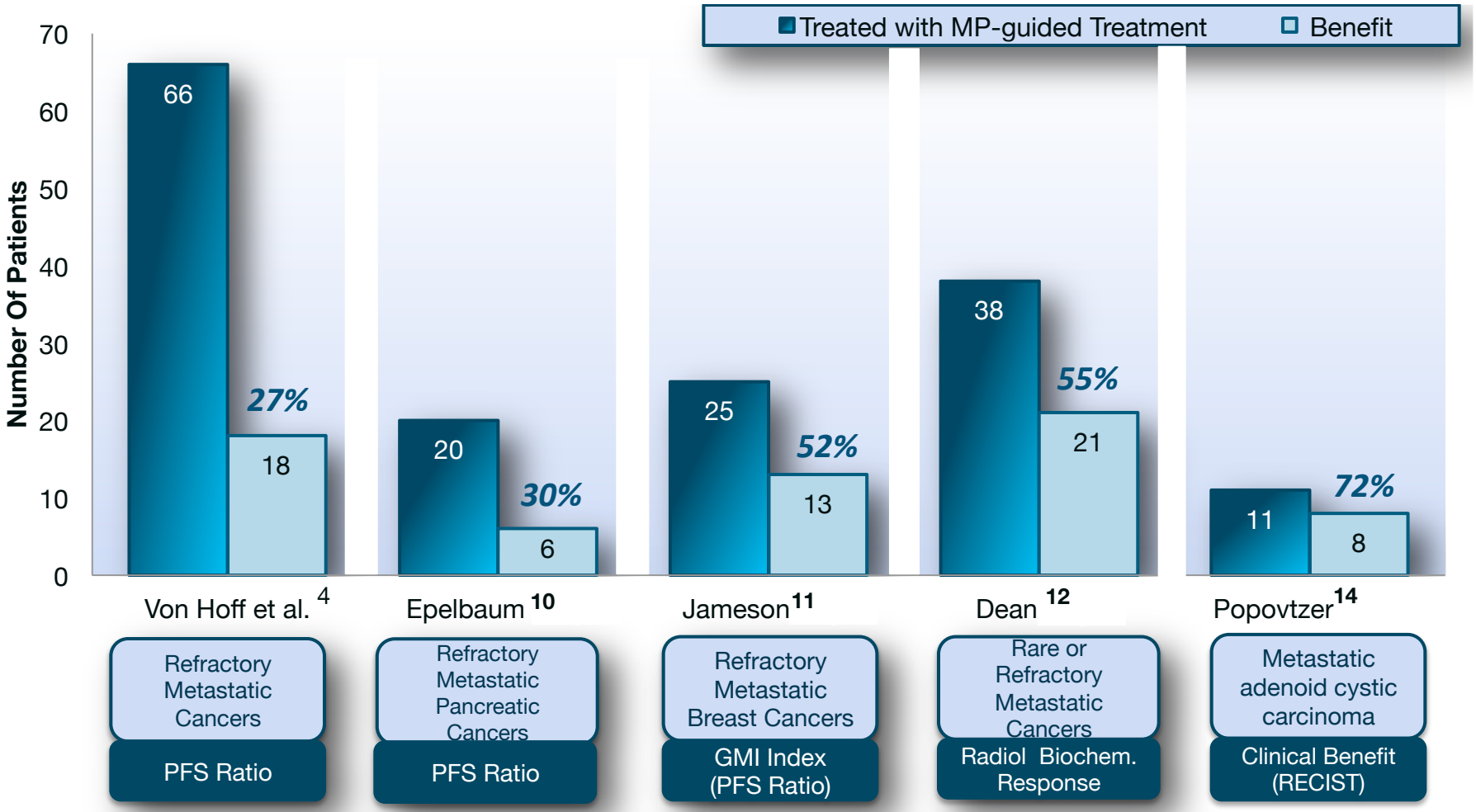


[16] Gabra H, ESGO Congress 2014, Poster #7

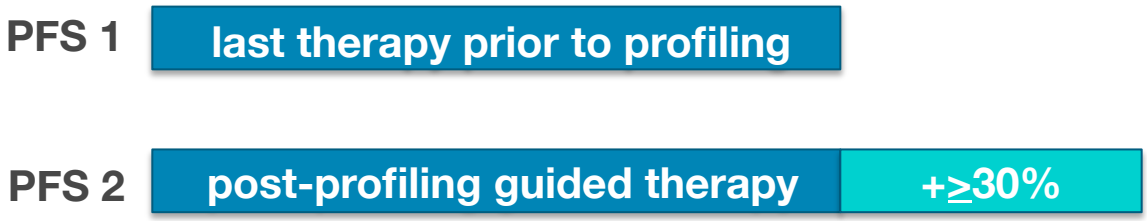
Most Patients profiled receive a MP guided treatment in clinical practice



Many patients who receive a profiling-guided treatment experience a measurable clinical benefit



Patients are considered to benefit from profiling guided treatment with a PFS increase of ≥ 30%

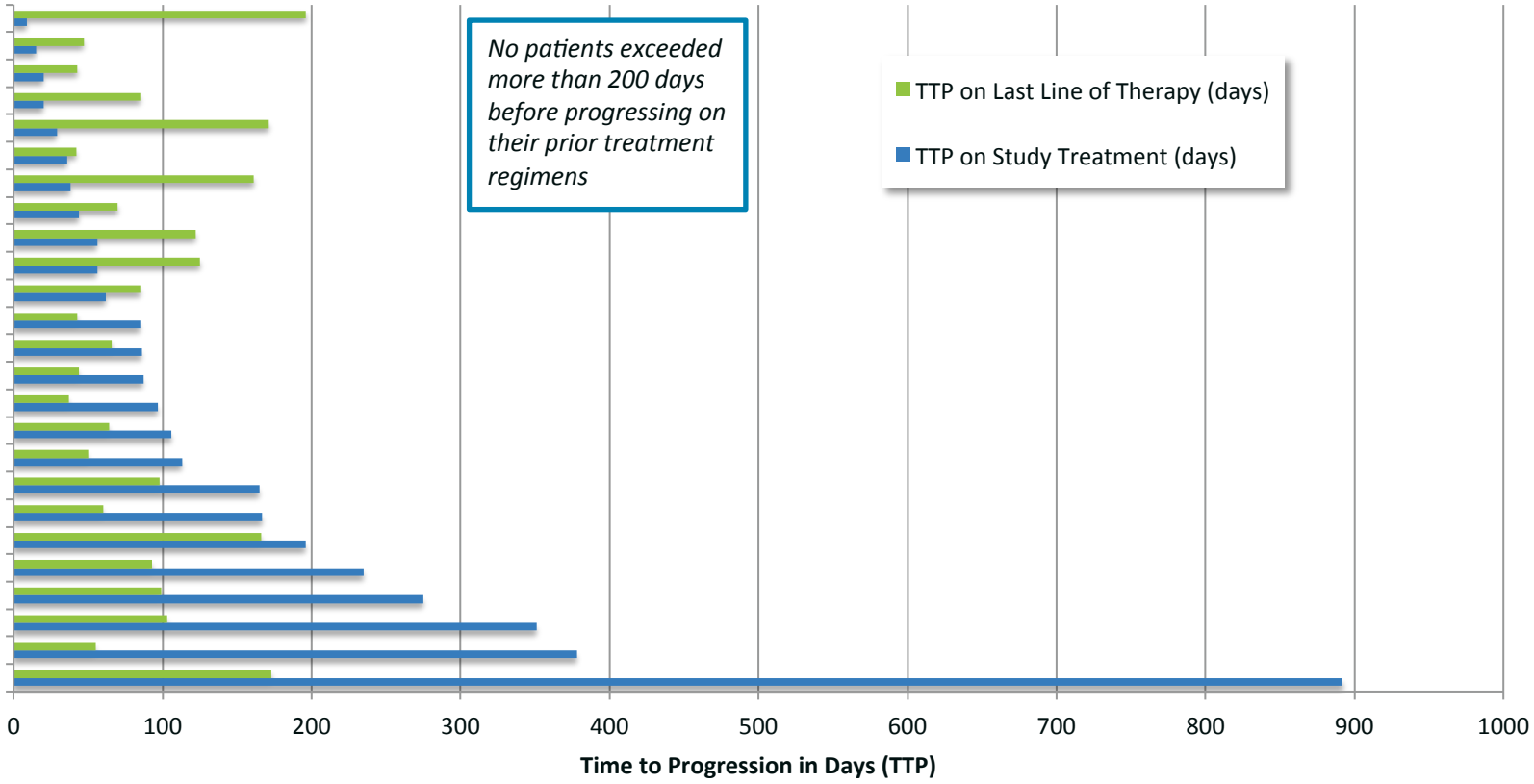


If the PFS2/PFS ratio is ≥ 1.3, profiling-guided therapy is defined in clinical trials as having benefit for patients[4,11,12].

A PFS ratio of ≥ 1.3 was shown in:

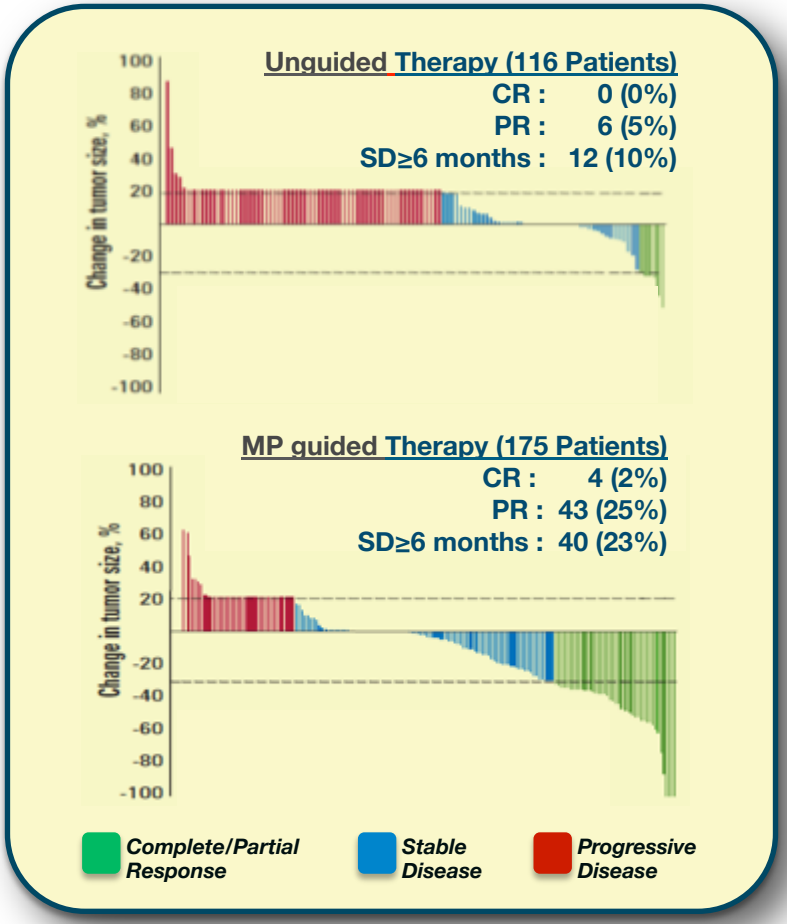
- **52%** (13/25) of patients with metastatic refractory breast cancer[12]
- **37.5%** (6/16) of patients with advanced pancreatic cancer[11]
- **27%** (18/66) of patients of a phase I population (various cancers)[4]

Comparison of PFS on profiling guided therapy vs prior therapy for patients with metastatic refractory breast cancer[11]



11) Jameson ASCO 2013

Tumour profile guided therapy improves outcomes when compared to unguided therapy



The MD Anderson Experience

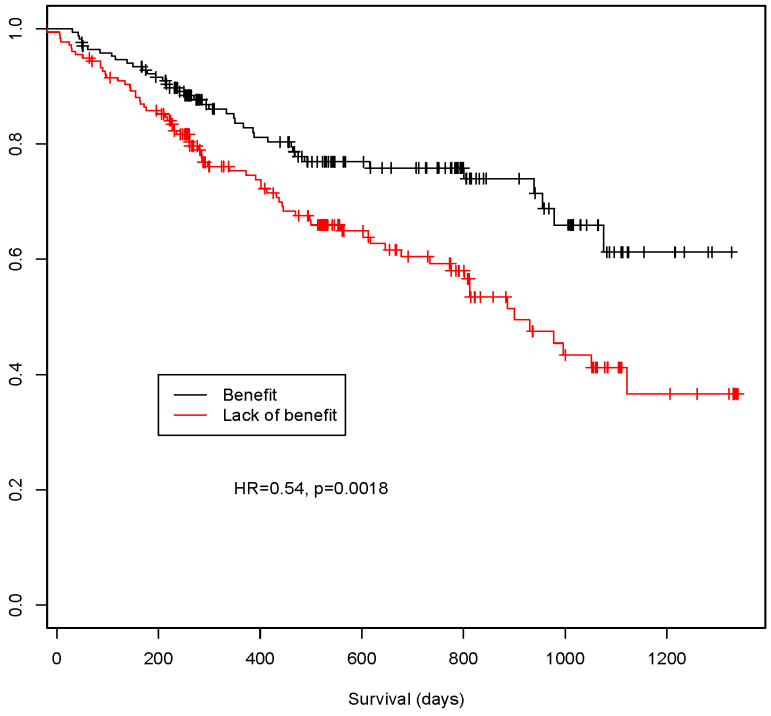
MP guided treatment was associated with **a higher overall response rate** (**27% vs. 5%**; P < 0.0001), **longer time-to-treatment failure** (TTF; P < 0.0001), and **longer survival** (median, **13.4 vs. 9.0** months; P = 0.017).

Tsimberidou D et al. 2012[13]

Note: retrospective analysis of patient outcomes after MP guided inclusion into phase I trials (limited panel assessed: PIK3CA, BRAF, KRAS, NRAS, GNAQ, MET, EGFR, KIT, and TP53)

Treatment in line with profiling results can improve post-profiling survival

Initial report from the Caris Registry™ [15]



- Patients with ovarian, fallopian tube, or primary peritoneal cancer patients were stratified based on the therapies they received:
- The "Benefit" cohort (n= 170) received at least one agent designated to be of potential benefit and no agents with potential lack of benefit while the "Lack of Benefit" cohort (n=178) received at least one agent with potential lack of benefit.
- Patients in the Benefit cohort experienced **significantly longer post-profiling survival**, as evidenced by a **46 percent reduction in the risk of death**, compared to the Lack of Benefit cohort (Hazard Ratio = 0.54, 95 percent CI 0.37-0.80; p=0.0018)[15].