Moving Early Diagnostics to Global Patients

- Advancing equitable cancer care through innovation

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SeekIn

Sept 16, 2022
Amsterdam

Cancer
- The emperor of all maladies

- A huge burden globally and will stay with human forever
- Significant progresses in the past 100 years especially in the last two decades
- Deep knowledge and improved outcome
- Precision cancer management has been taking place in top academic centers
- Expenditure becomes another burden on the public healthcare systems and the families
- Accessibility, affordability and equity are huge challenges

The perspectives

Advancing equitable cancer care through innovation

- Scalable
- Cost-effective
- Convenience

Prevention, Diagnosis and Treatment

Blood tests for getting right treatments at earlier time

思康宁®

SeekIn Care®

Pan-cancer early detection

SeekIn Cure™

思康安®

Pan-cancer Recurrence monitoring

SeekInClarity™

Pan-cancer Treatment Response monitoring

思康明®

Indicated subjects:	Healthy population	Post-op patients of radical resection	Late-stage patients
Launch date:	Nov. 2018	May 2019	Aug. 2020

One-Size-Fits-All

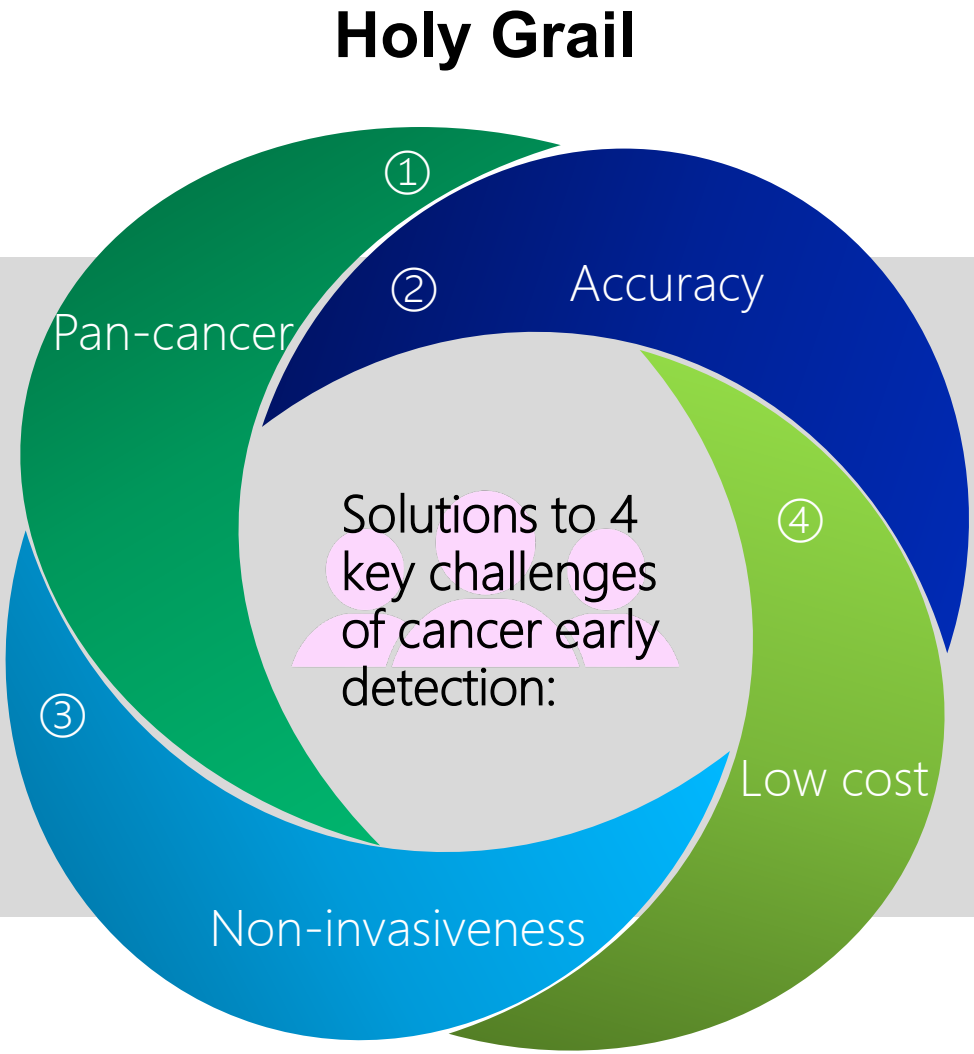
SeekIn has dedicated to figure out solutions to key challenges

Mission

- Detecting cancer early when it is still curable

Vision

- Leading novel screening approaches to reduce cancer mortality by 15% in screened population by 2030



seek and you will find – Matthew 7:7

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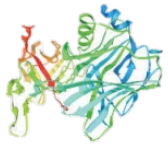
“top-down” approach

Conventional	Single cancer type	Multi-cancer types	Pan-cancer
4-5 cancer types High-risk population Low accuracy Invasive	One cancer type High-risk population Complementary to SOC screening Noninvasive	>5 cancer types Average-risk population Bottom-up approach High cost	Pan-cancer Average-risk population Top-bottom approach Cost-effective



Level 0

CT, B ultrasound,

Cytology, Protein markers

cologuard Rx only

COLOCLEAR 常卫清

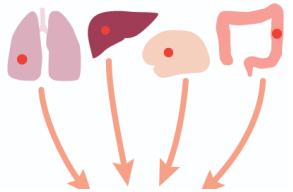
Level 1

<5 markers

Galleri™

Level 2

10^6 markers



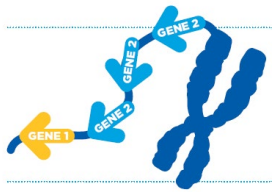
“Bottom-up”:
Add up the markers of individual cancer types

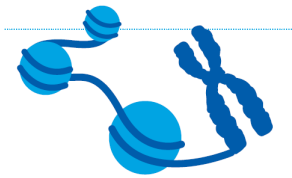
SeekInCare®

Level 3

Whole genome

3 billion bases





“top-down”:
Utilize common features for all cancer types

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The path finding study

Detection of asymptomatic cancers by shallow genome sequencing and 7 protein markers in ~2 million pregnant women (2016-2017)

Genetics inMedicine

View all journals | Search | Login

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nature > genetics in medicine > articles > article

Article | Published: 12 April 2019

Identifying occult maternal malignancies from 1.93 million pregnant women undergoing noninvasive prenatal screening tests

Xing Ji MD, Jia Li PhD, ... Mao Mao MD, PhD + Show authors

Genetics in Medicine **21**, 2293–2302 (2019) | Cite this article

seek and you will find – Matthew 7:7

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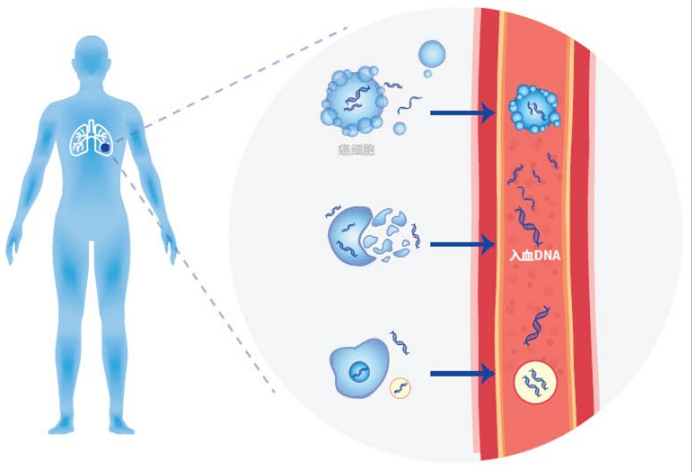
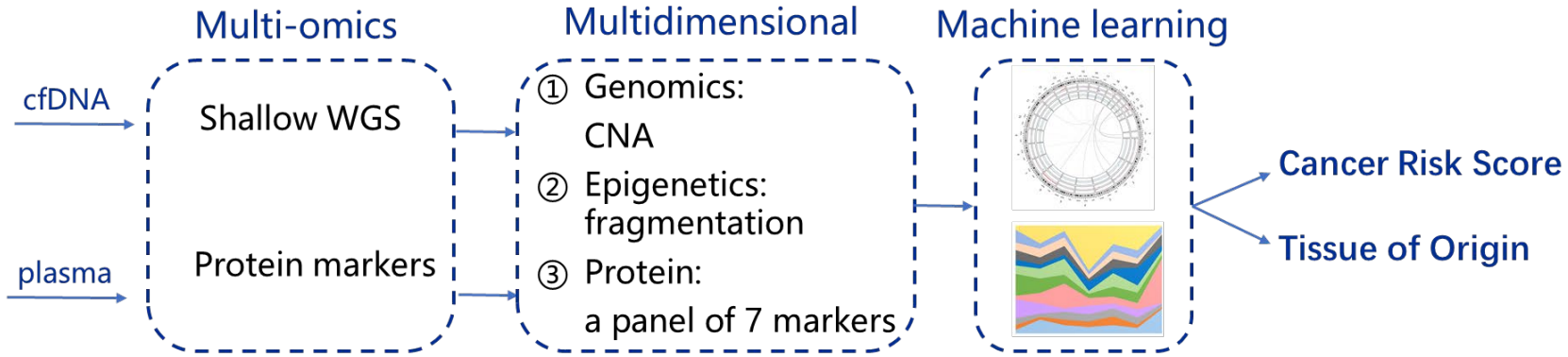
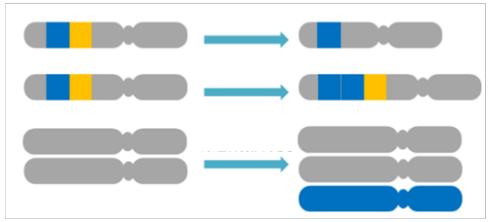
Technical edge



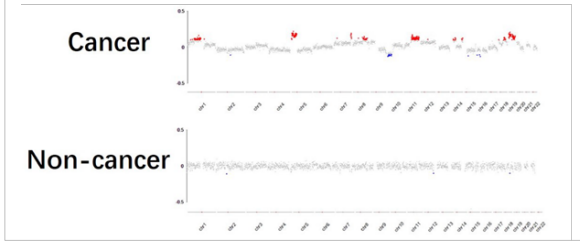


We capture the cancer genomic landscape via a panoramic view by shallow WGS. Thus cancer hallmarks such as CNA and fragment size in conjunction with protein biomarkers can be utilized to refine the MCRS model.

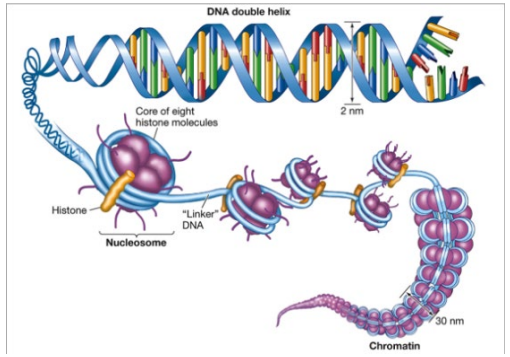
① Copy number aberration (CNA)

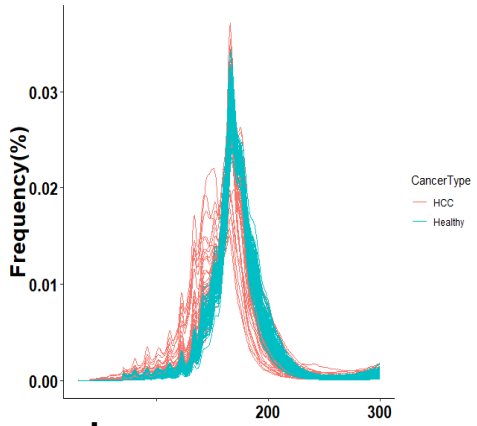


CNA analysis from cfDNA sWGS



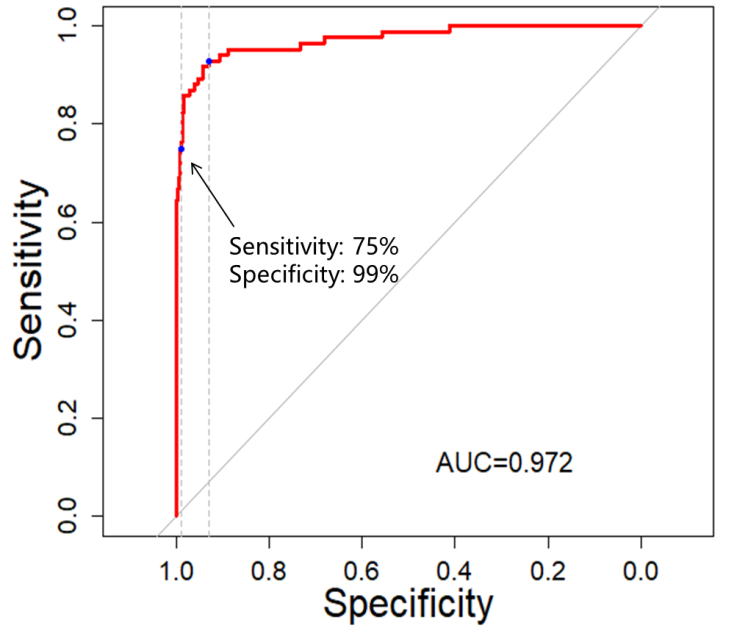
② Fragmentation





③ Protein markers

AFP, CEA, CA199, CA125, CA153, CA211, CA724



Product – SeekInCare®

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SeekInCare®

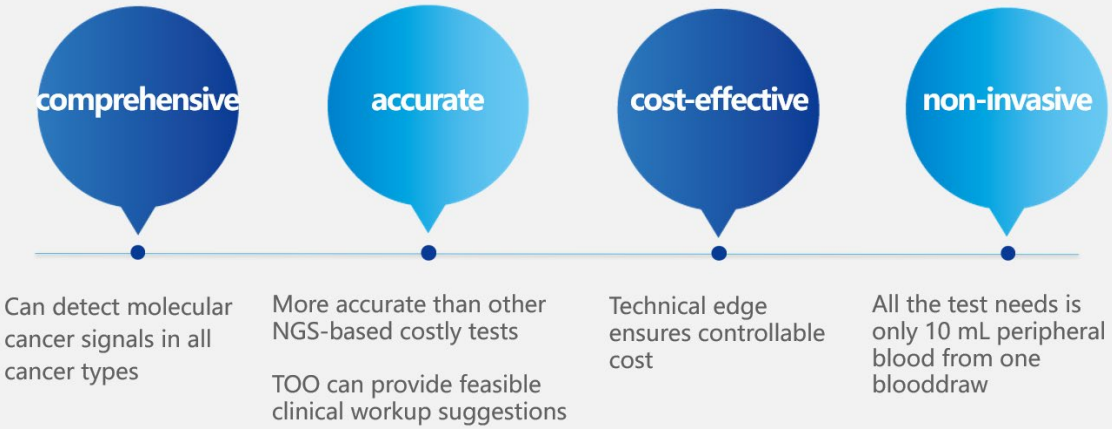
the first-in-class blood-based pan-cancer early detection test

CE Marking

A panoramic view of cancer genomics landscape + protein markers

Big data + AI

A blood-based test generating CRS and locating TOO



" An inborn pan-cancer early detection test"

Methodology paper: Meng Z, et al. Non-invasive detection of hepatocellular carcinoma with circulating tumor DNA features and AFP. J Mol Diagn. 2021 Sep;23(9):1174-1184.

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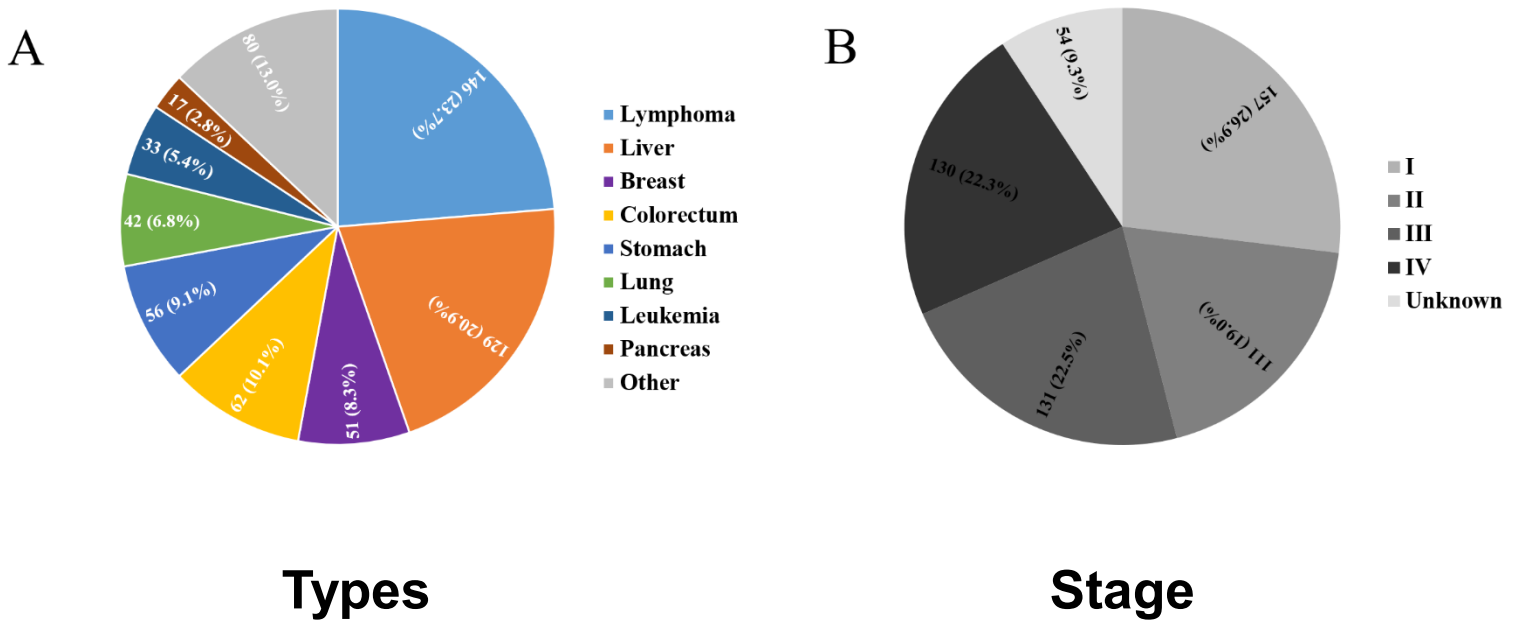
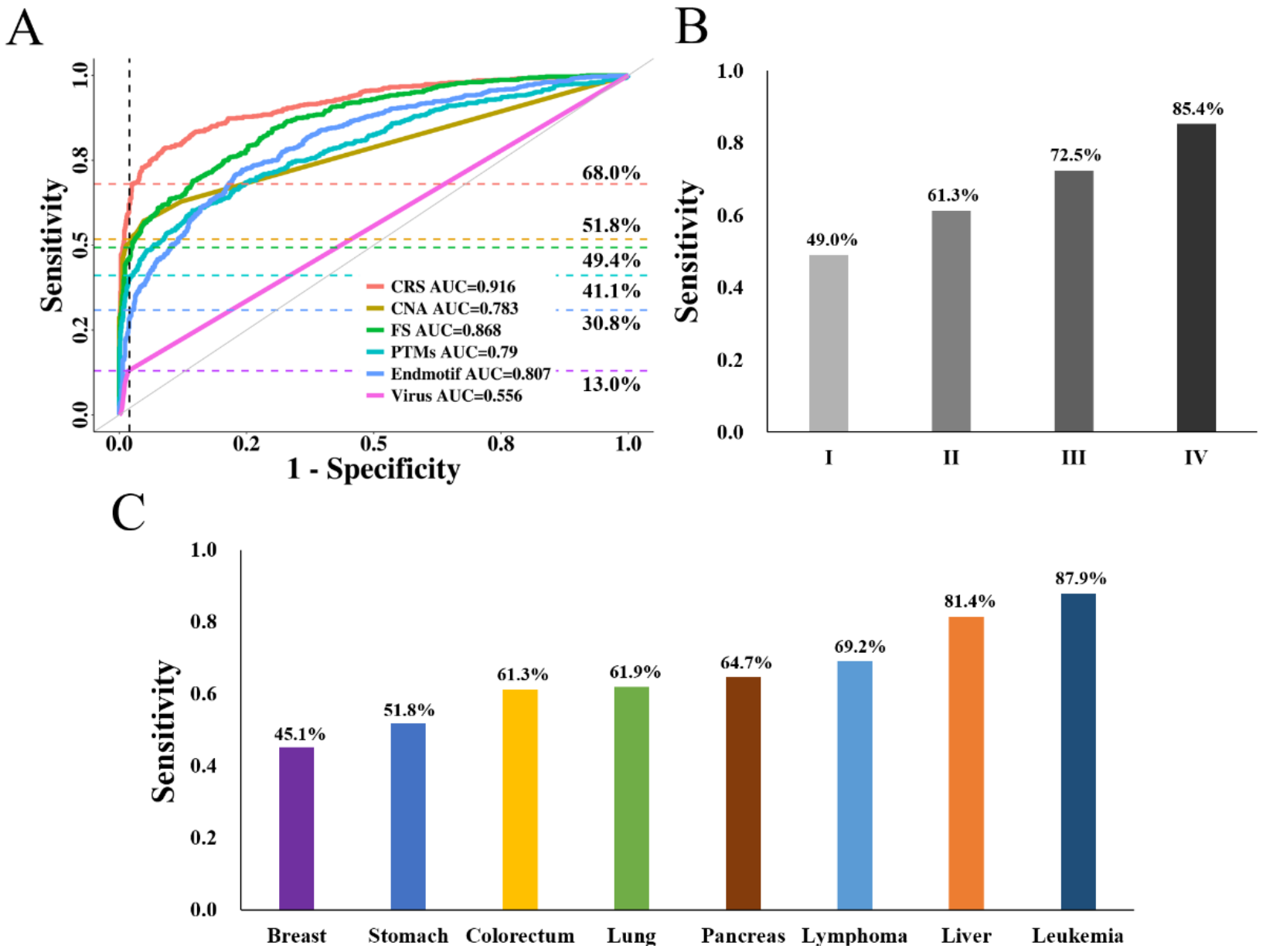
The 2nd validation study

616 stage I-IV cancer patients that cover eight common cancers and the other types and 898 healthy subjects.

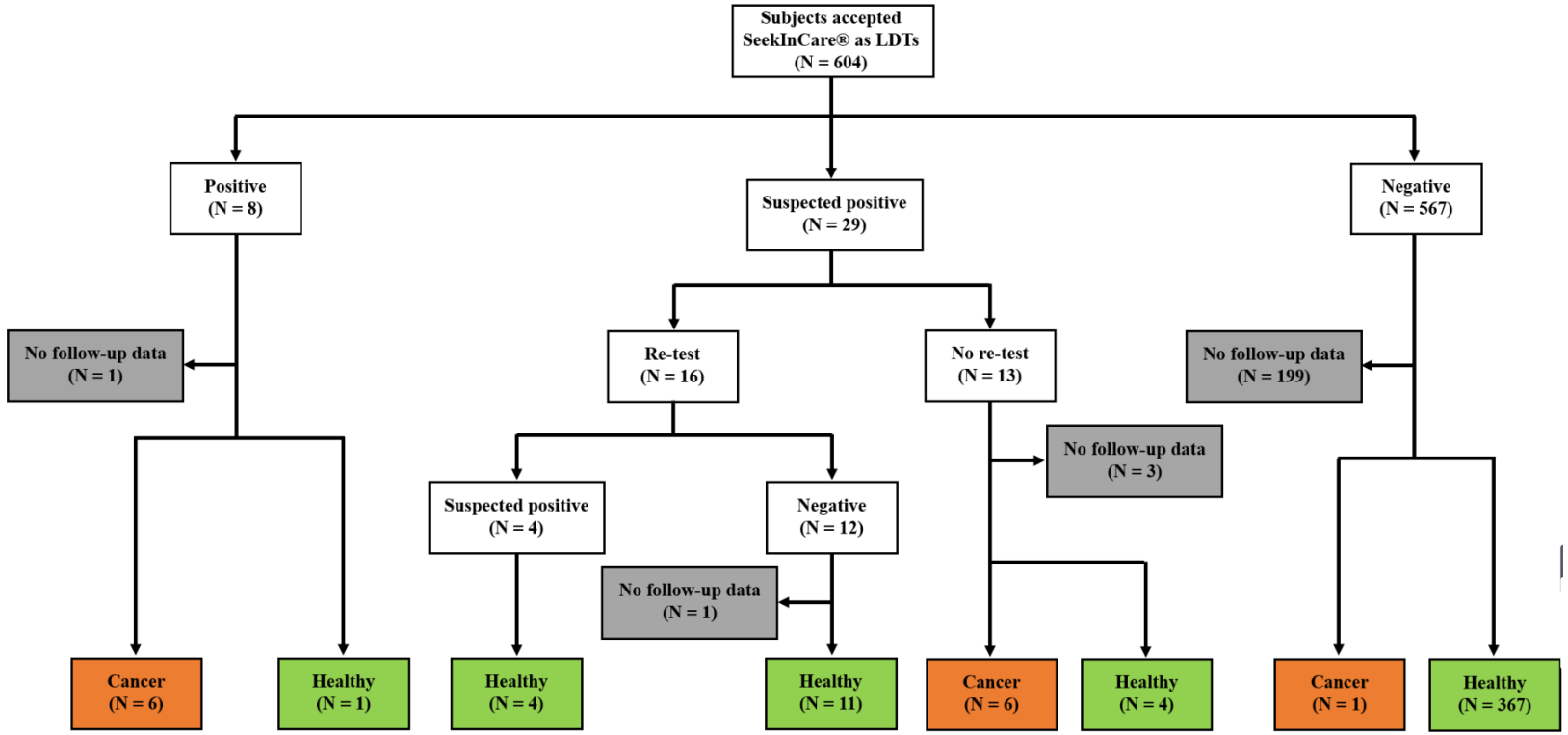


Types **Stage**

Performance of SeekInCare® in the 2nd validation study



Performance of SeekInCare® in the real world



92.3% sensitivity, 97.8% specificity, 48% PPV and 99.8% NPV

Low-cost cancer detection: OncoSeek®

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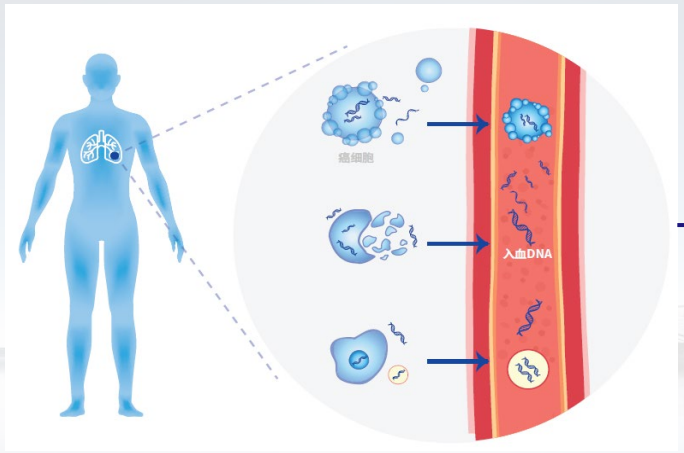
OncoSeek®

CE Marking

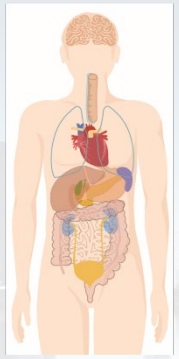
OncoSeek®, a combination of 7 clinically validated plasma tumor markers (AFP, CA125, CA15-3, CA19-9, CA72-4, CEA, and CYFRA21-1), using a new multivariate OncoSeek algorithm combined with big data and AI, performs early detection for 12 common cancers by calculating the probability of cancer (POC) and tracing the cancer tissue of origin (TOO).

Bladder	Breast	Cervix	Colorectum	Esophagus	Gallbladder
Liver	Lung	Ovary	Pancreas	Stomach	Testis



plasma

Bladder: CEA
Breast: CA15-3, CEA
Cervix: CEA
Colorectum: CEA, CA19-9
Esophagus: CEA
Gallbladder: CA19-9, CEA



Liver: AFP, CA19-9, CEA
Lung: CEA, CYFRA21-1
Ovary: CA125
Stomach: CEA, CA19-9, CA72-4
Pancreas: CEA, CA19-9
Testis: AFP

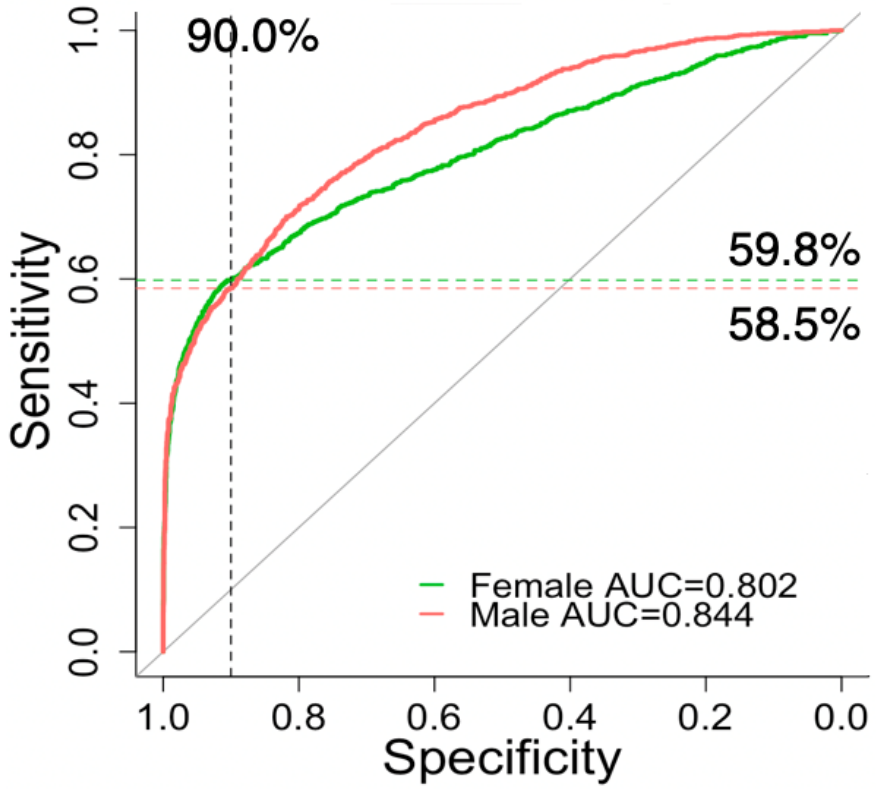
Protein marker panel

OncoSeek V1.0

Machine learning

POC
TOO

Low-cost cancer detection: OncoSeek®



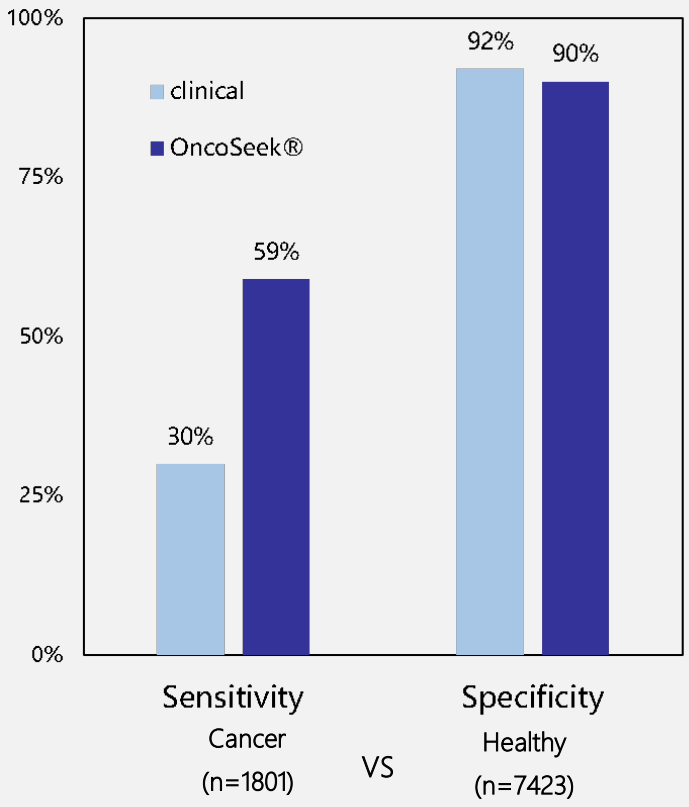
	Female		Male	
	Cancer	Healthy	Cancer	Healthy
Predicted cancer	518	341	547	400
Predicted noncancer	348	3075	388	3607
Sensitivity % (95% CI)	59.8 (56.5—63.1)		58.5 (55.3—61.7)	
Specificity % (95% CI)	90.0 (89.0—91.0)		90.0 (89.0—90.9)	
PPV % (95% CI)	60.3 (56.9—63.6)		57.8 (545—60.9)	
NPV % (95% CI)	89.8 (88.8—90.8)		90.3 (89.3—91.2)	

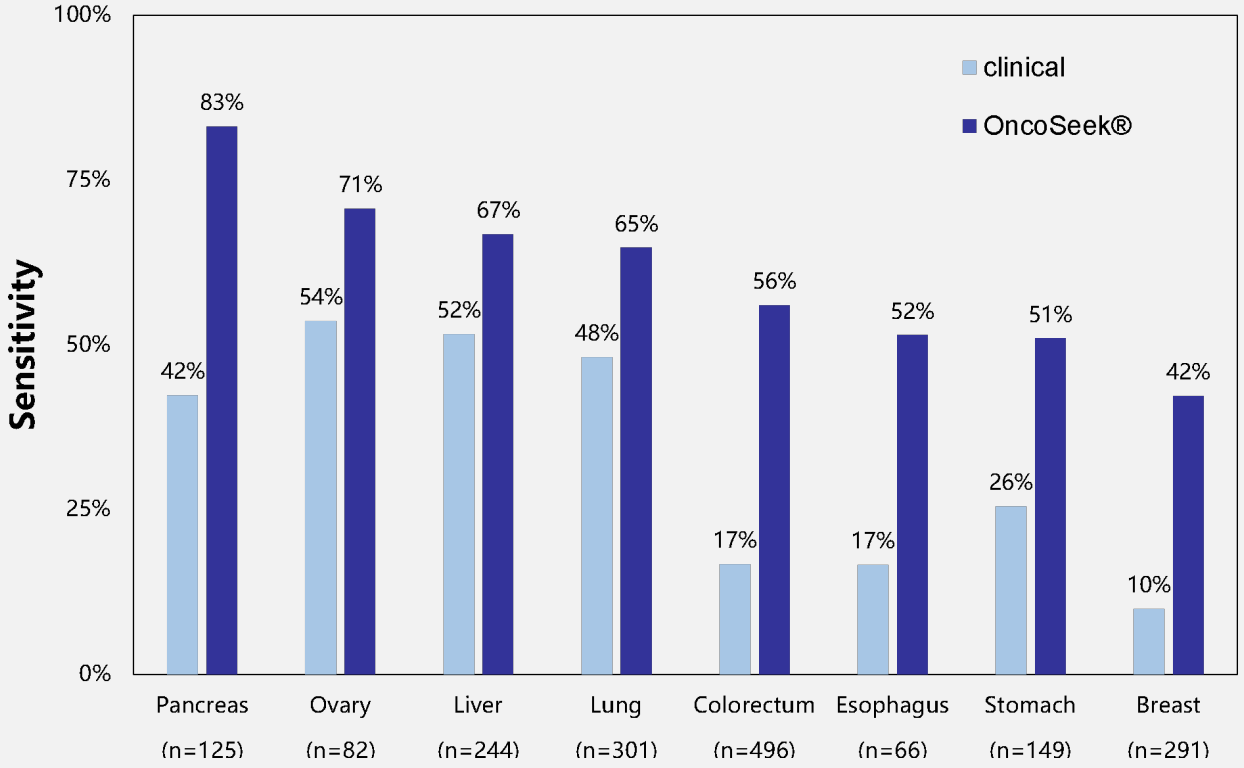
✓ Using US FDA/CE/NMPA approved reagents and instrument (Roche cobas e411) to improve the accuracy of cancer detection

✓ Based on the analysis of ~10,000 blood samples, the sensitivity of OncoSeek was ~60% at 90% specificity, and the AUC was greater than 0.80

Low-cost cancer detection: OncoSeek®

Based on the analysis of nearly 10,000 samples, with specificity at ~90%, the sensitivity of OncoSeek® (59%) for cancer detection is two times more than that of using current clinical method.





Recurrence monitoring - SeekInCure™

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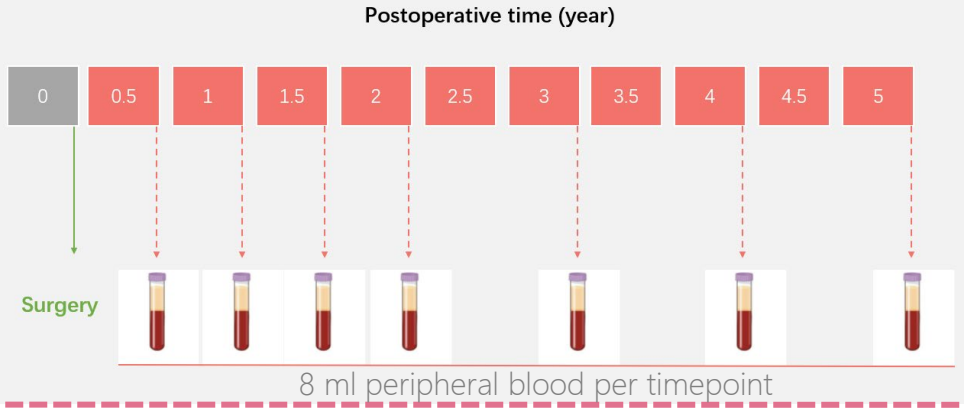
CE Marking

SeekInCure™ is applied to monitoring cancer recurrence and risk evaluation for post-op cancer patients. By monitoring the variation of cancer genome in cell-free DNA (cfDNA) of post-op cancer patients continually, combined with plasma protein markers, equipping big data and artificial intelligence, it generates cancer recurrence index (CRI) .

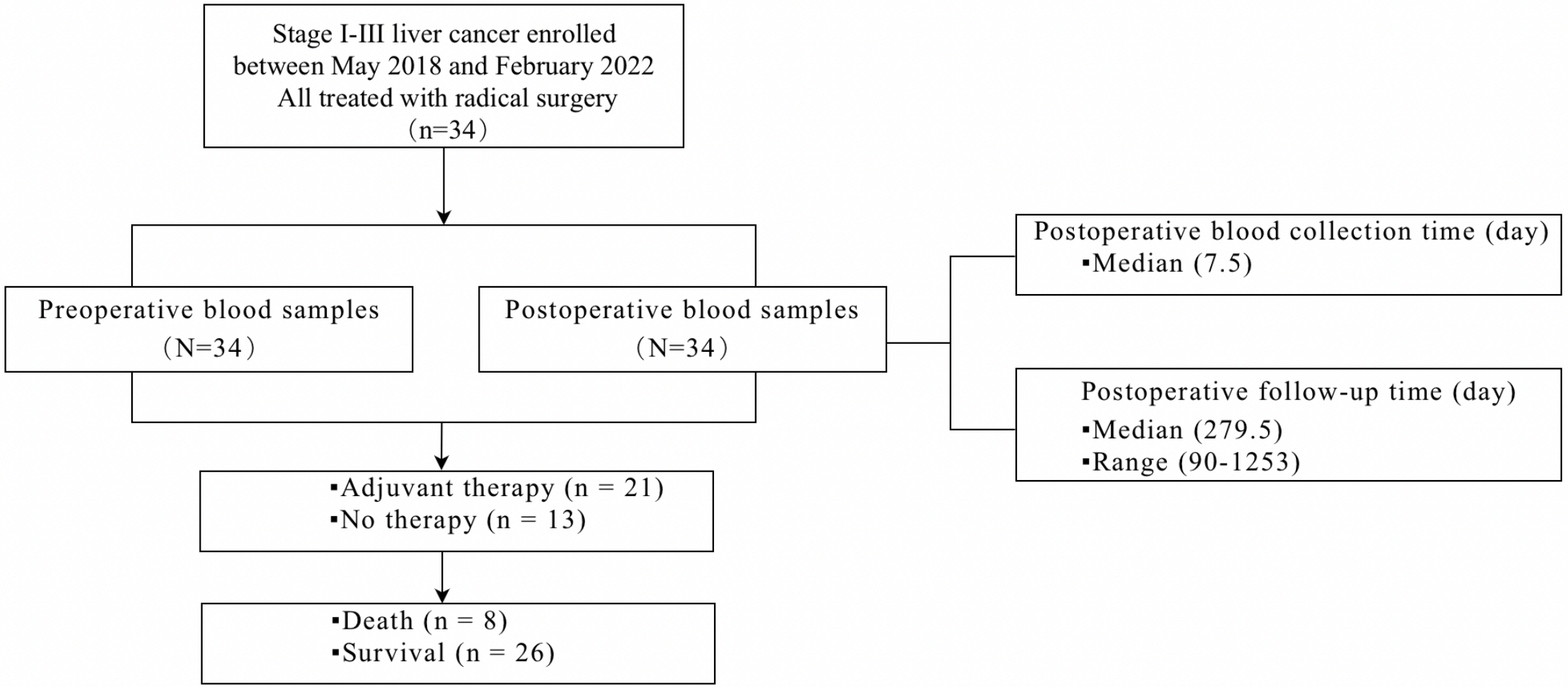


Characteristics

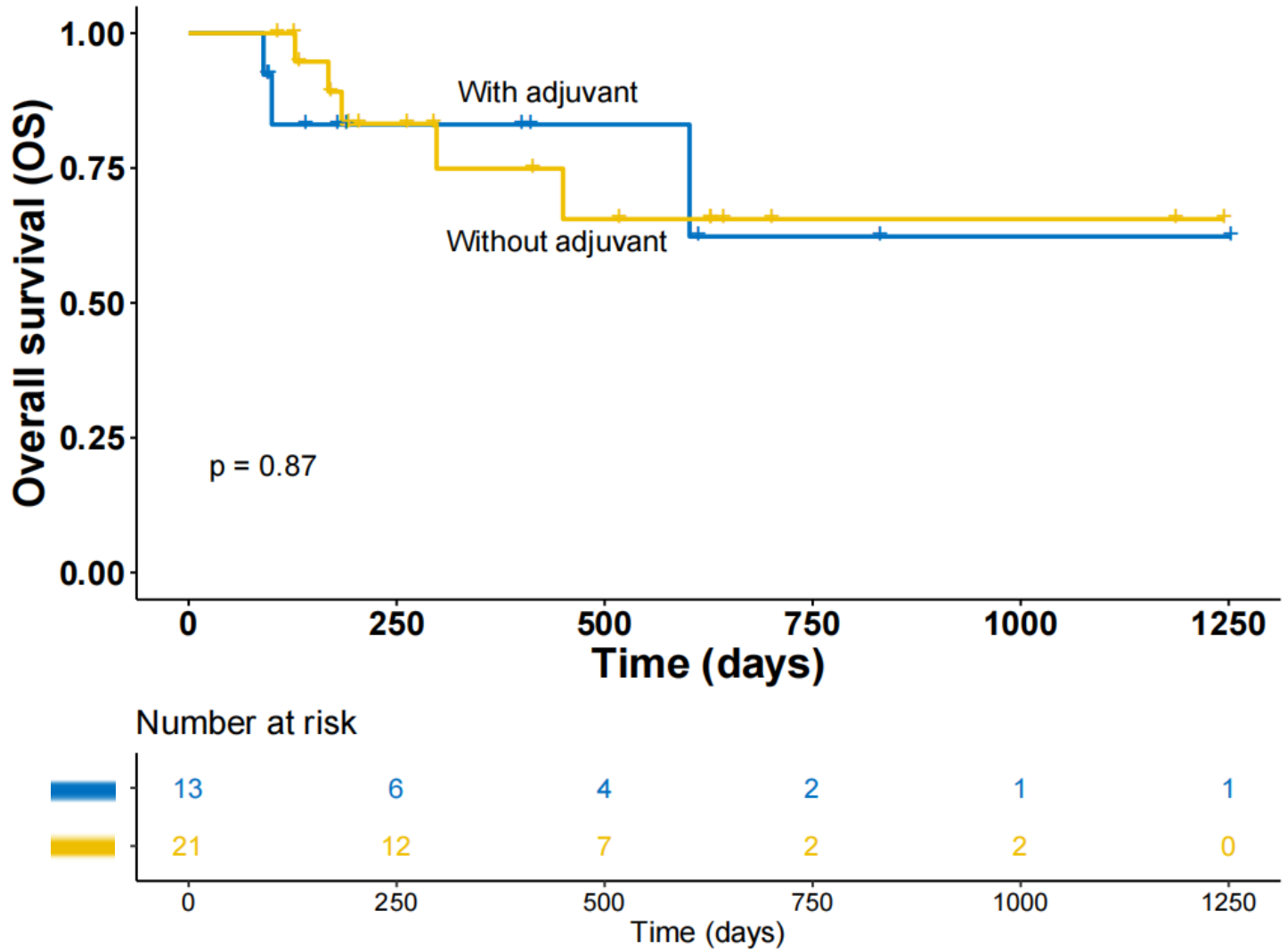
- Precise → Personalized surveillance
- Non-invasive → Blood-based
- Broad-spectrum → Primary/Metastatic cancerous lesions
- Multi-omics → sWGS+ protein markers
- Cost-effective → Affordable

SeekInCure™ – HCC prospective MRD study

Prospective HCC MRD study (2018.05 ~ 2022.02)：enrolled HCC radical surgery patients.
8ml blood sample collected at preoperative (treatment-naive) and postoperative timepoints.



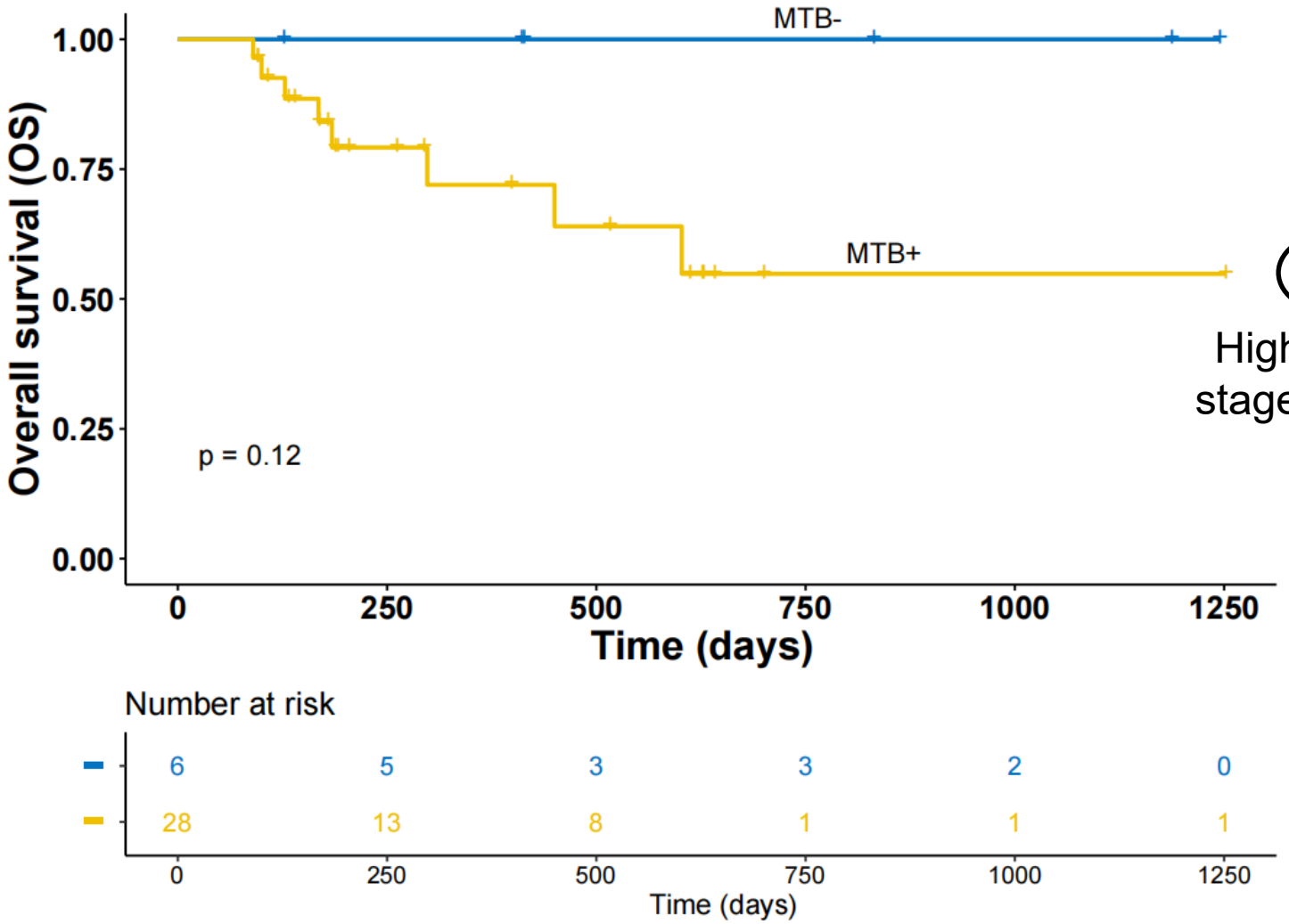
Adjuvant has no influence on survival



To be treated or not to be?

SeekInCure™ – preoperative

SeekInCure MTB detection for prognosis



18%

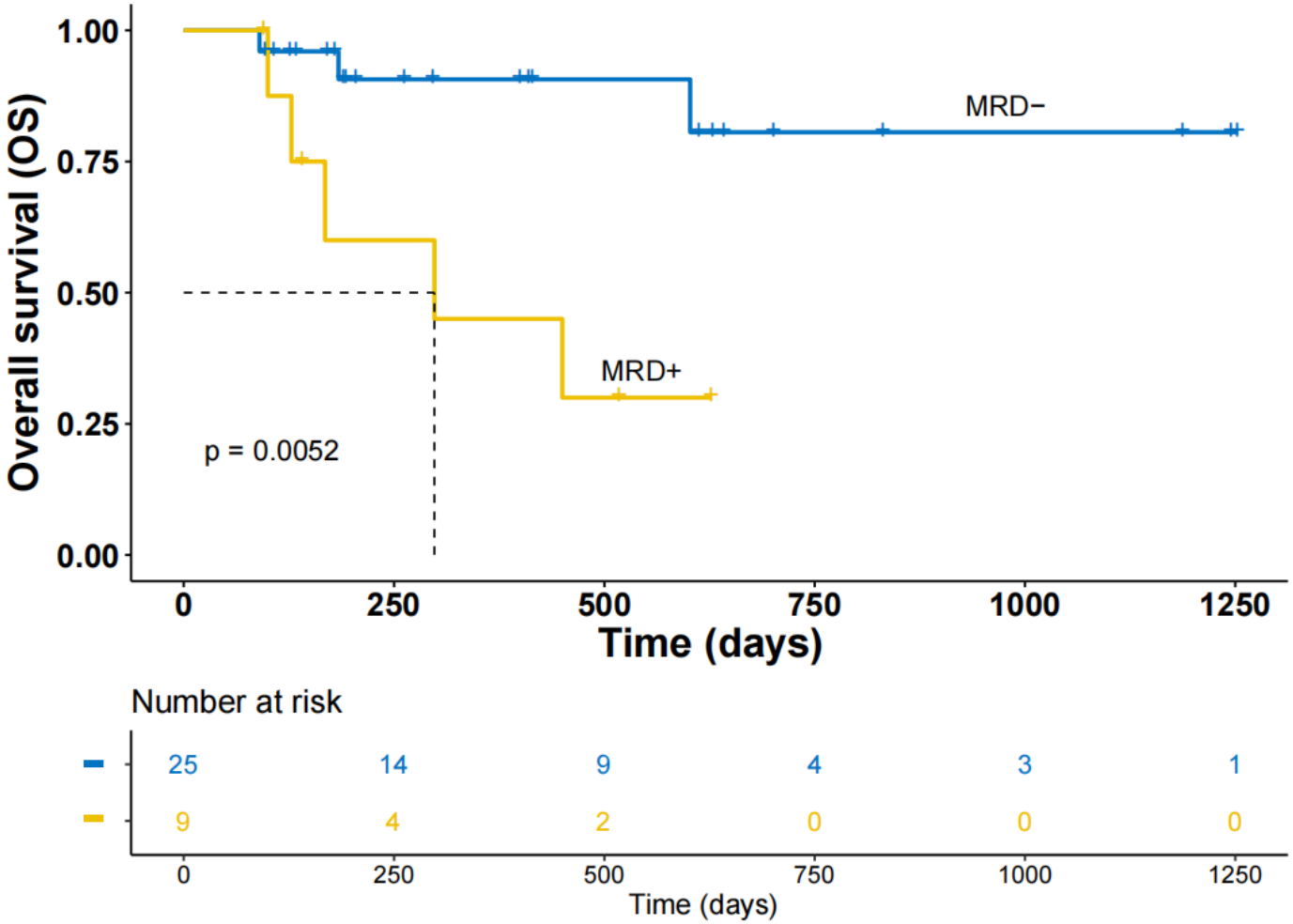
82%

High sensitivity in this early stage dominated HCC cohort

MTB: molecular tumor burden. MTB+/-: molecular signal of tumor is detectable/undetectable

SeekInCure™ – postoperative

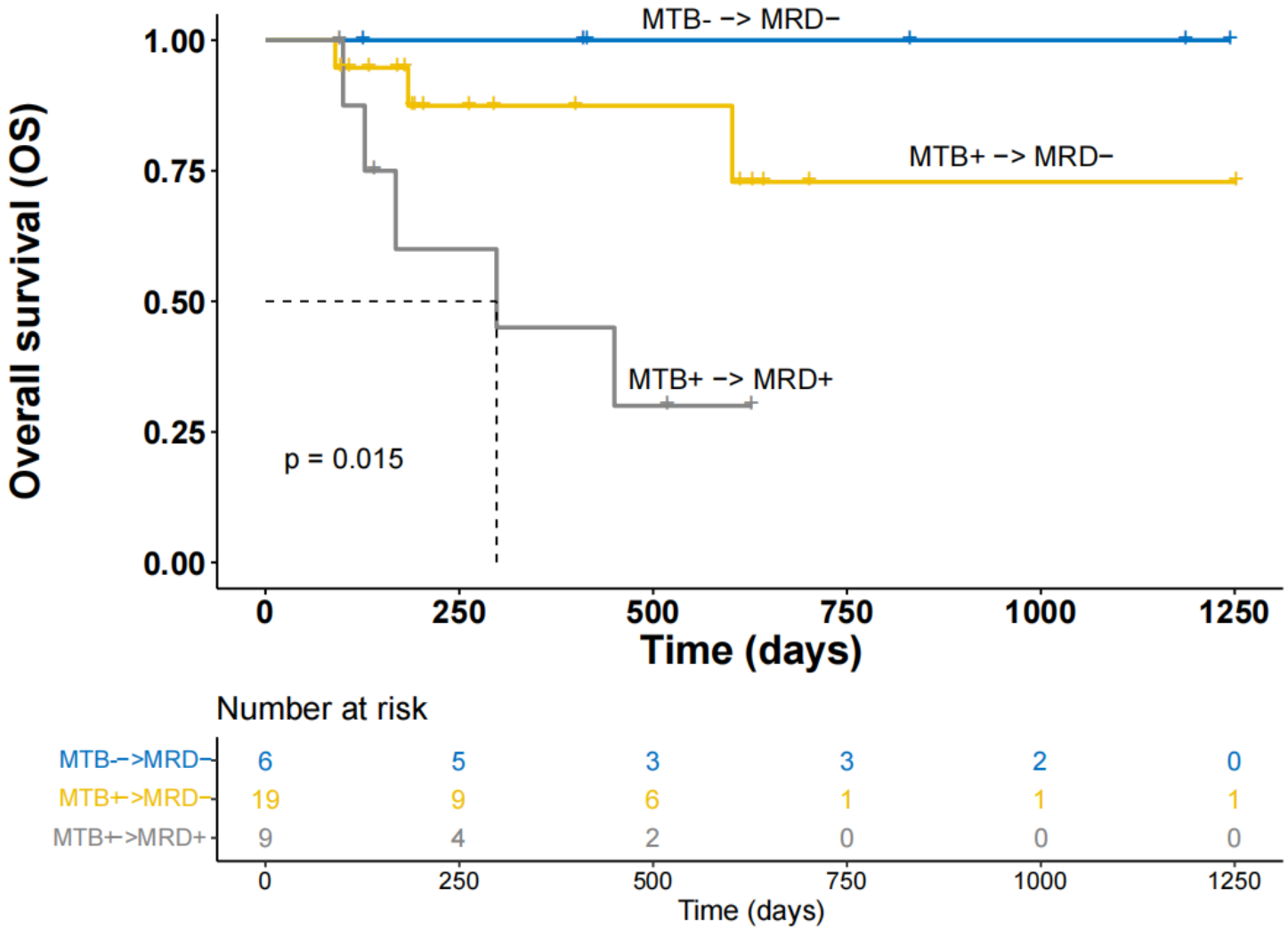
SeekInCure MRD detection for prognosis



After surgery, patients with MRD+ have shorter survival time.
Median overall survival time is less than 1 year.

Pre-/post- operative changs and outcome

Patients who are MTB- and MRD- have very good OS



31% MTB+ patients remained positive (i.e. MRD+) after surgery

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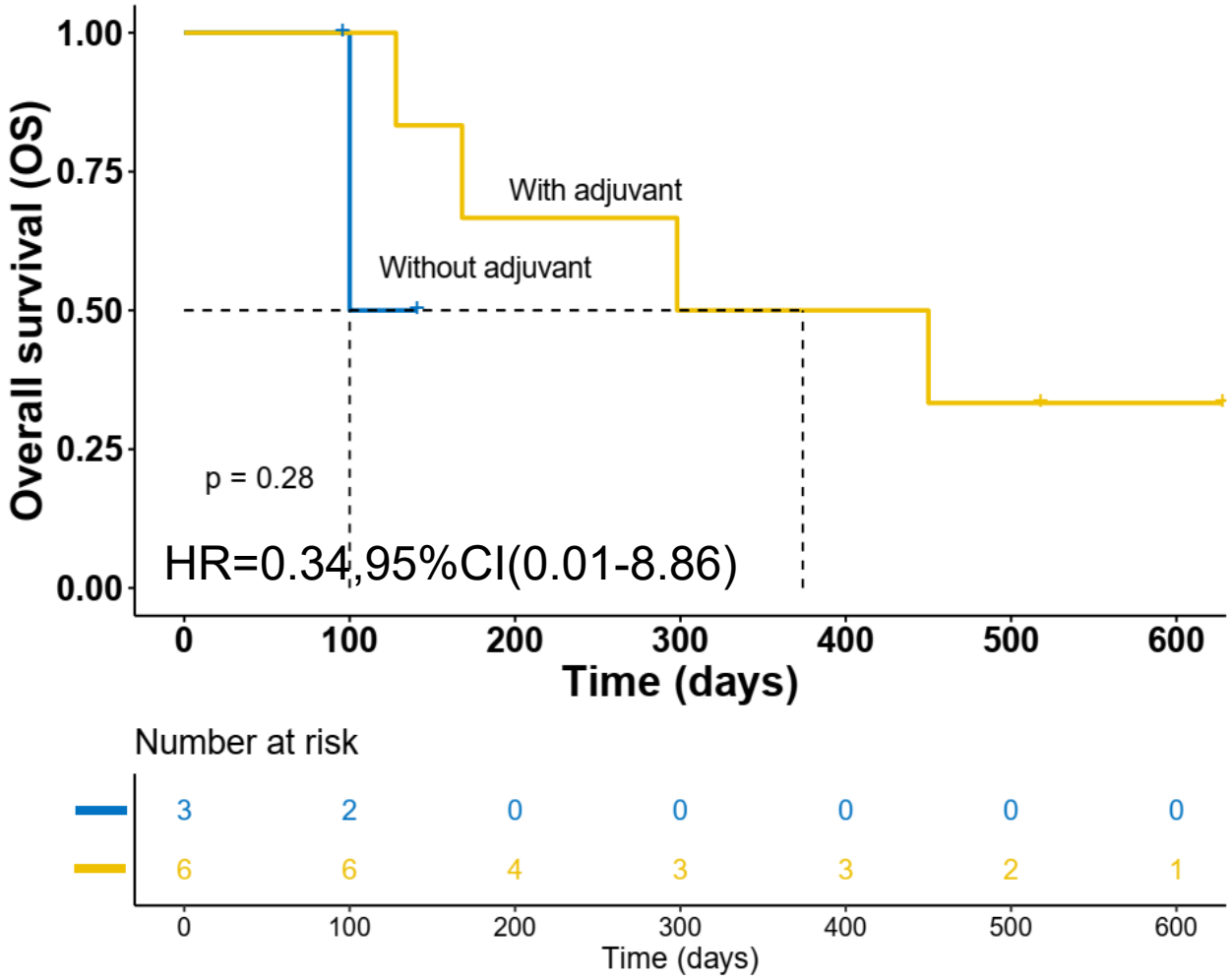
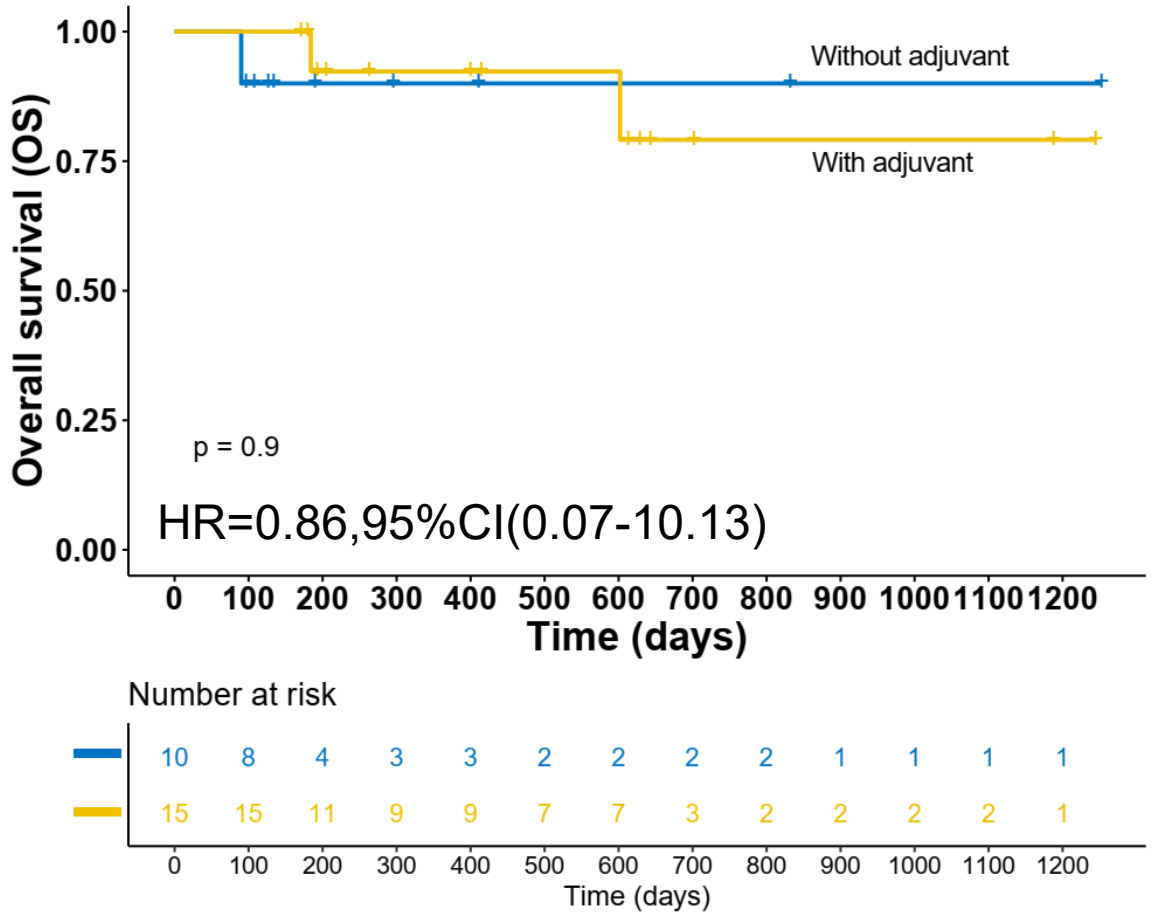
SeekInCure™ – with/without adjuvant

Under MRD+ group



Under MRD- group



Among HCC MRD- group, adjuvant has no influence on survival

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SeekInCure™ – summary

- SeekInCure is a cost-effective pan cancer MRD test that does not require cancer tissue analysis.
- Both preoperative MTB and postoperative MRD values are prognostic.
- Double negative (MTB- and MRD-) patients have a very favorable outcome (100% OS).
- Double positive (MTB+ and MRD+) patients have the worst outcome (median overall survival time is less than 1 year).
- Adjuvant has no influence on survival，especially in MRD- patients.

Response monitoring - SeekInClarity™

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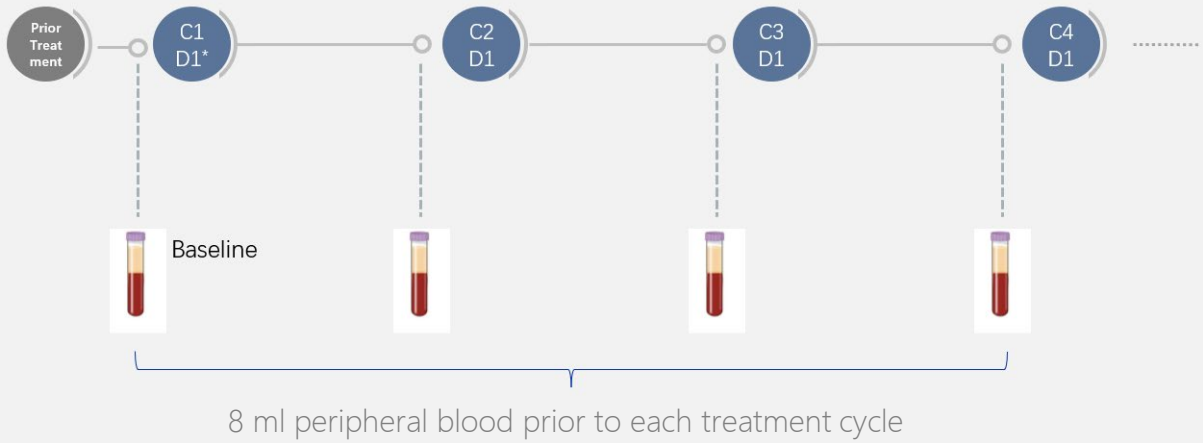
SeekInClarity™

CE Marking

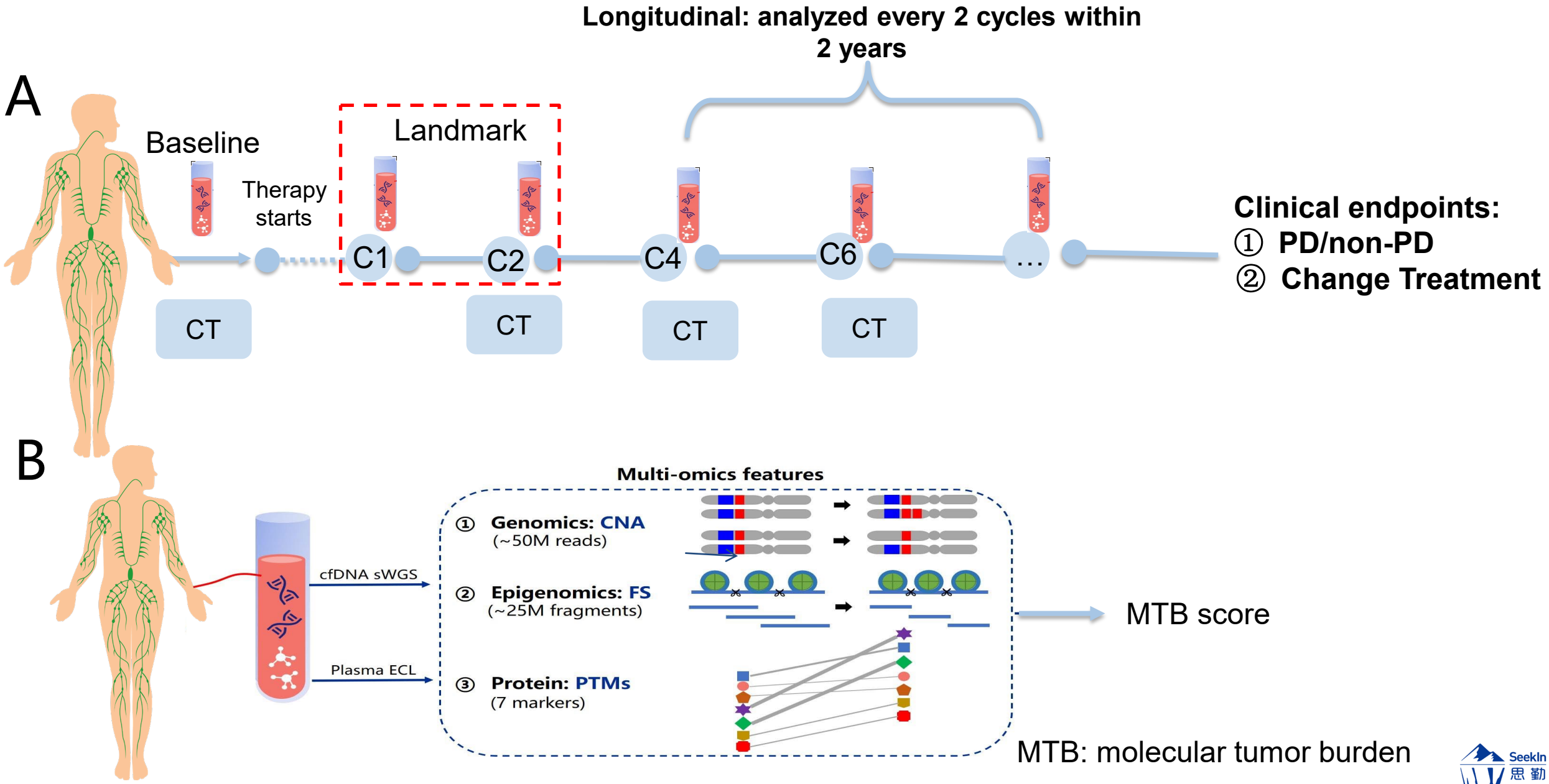
- √ Pan-cancer
- √ Pan-indication
- √ Multi-omics
- √ Prompt monitoring

SeekInClarity™ is the first-in-class blood-based pan-cancer pan-indication treatment response monitoring test, which uses a cutting edge multivariable molecular tumor burden (MTB) algorithm. Molecular response index (MRI) model maps the panoramic cancer genome by shallow whole genome sequencing (sWGS) data, evaluates the copy number aberration (CNA), fragment size (FS) and 7 plasma protein markers, to predict tumor burden and therapeutic efficacy of the late-stage cancer patients during treatment including chemotherapy, target therapy and immunotherapy or combination therapies.



*: Cycle 1 Day 1, the 1st day of each treatment cycle

SeekInClarity™ for lymphoma treatment response



Clinical summary of lymphoma patients

Characteristics	No. (%)
No. of patients	154
Median age, years (range)	55 (13, 81)
Sex	
Female	82 (53.2)
Male	72 (46.8)
Subtype	
DLBCL	64（41.6）
NK/TCL	20（13）
HL	14（9.0）
FL	11（7.1）
AITL	8（5.2）
Others	37（11.7）
Stage	
Ⅰ	27（17.5）
Ⅱ	30（19.5）
Ⅲ	17（11.0）
Ⅳ	73（47.4）
NaN	7（4.5）

Regimens	
R-CHOP	27（21.8）
R-CDOP	17（13.7）
PD-1	9（7.3）
BR	9（7.3）
DDGP	9（7.3）
AVD	6（4.8）
CHOP	5（4.0）
CDOP	4（3.2）
Other regimens	32（25.8）
NaN	6（4.8）

114 patients were included in the interim analysis

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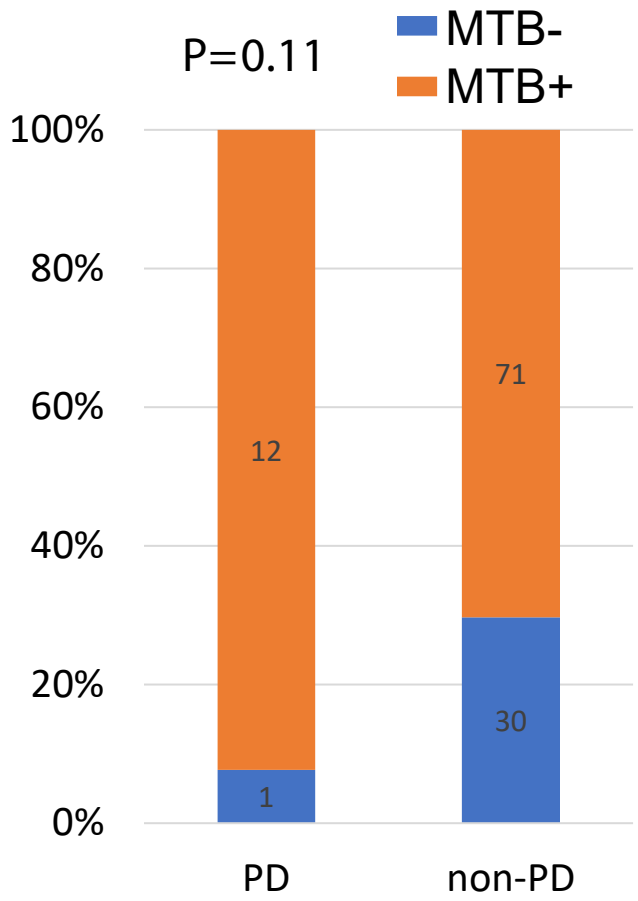
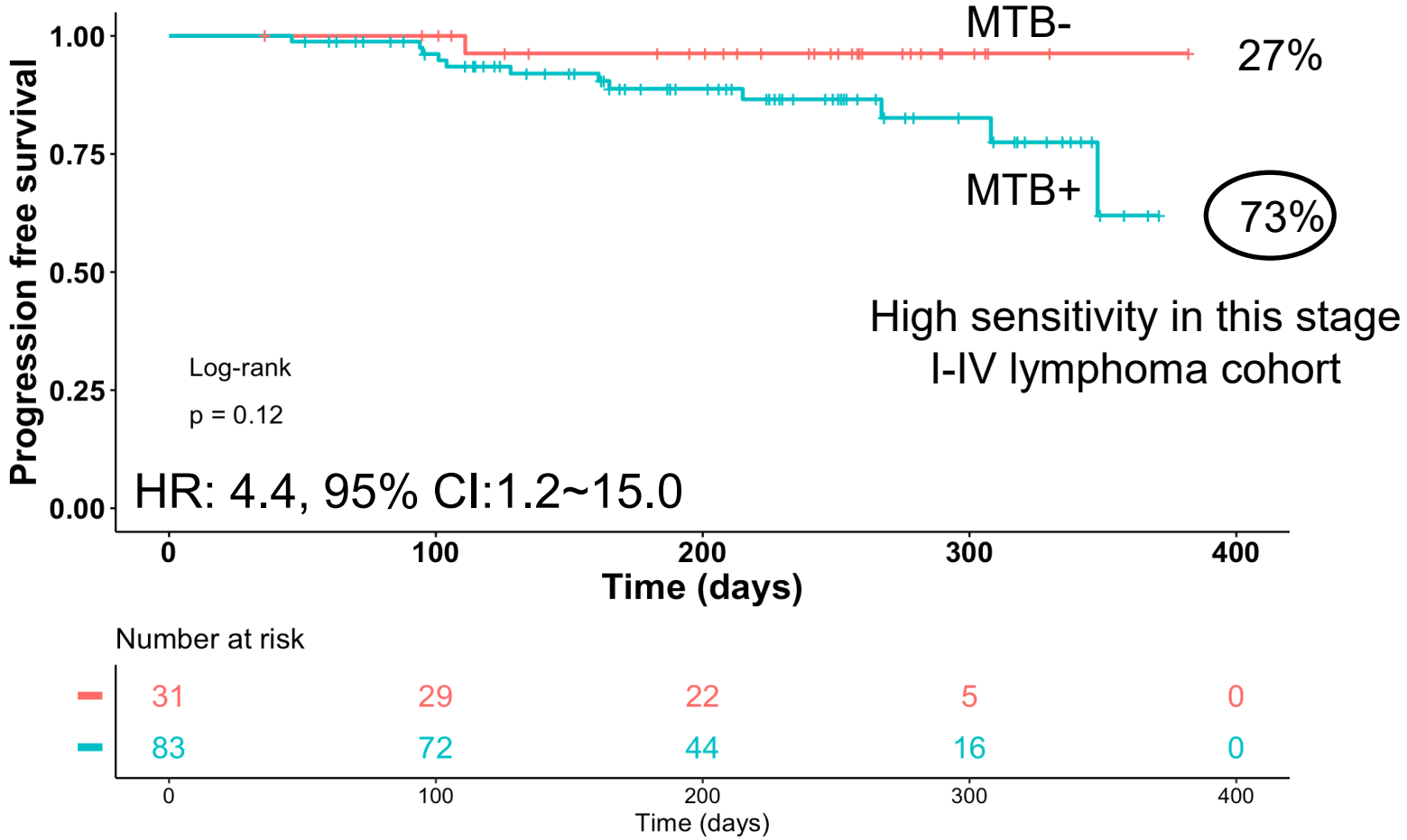
SeekInClarity™ analysis at baseline

Correlation between MTB status at baseline and clinical outcome (PFS)





High sensitivity in this stage I-IV lymphoma cohort

PD: Progressive disease, i.e. non-responders
Non-PD: responders, including SD, PR, CR

MTB: molecular tumor burden
MTB+/-: molecular signal of tumor is detectable/undetectable

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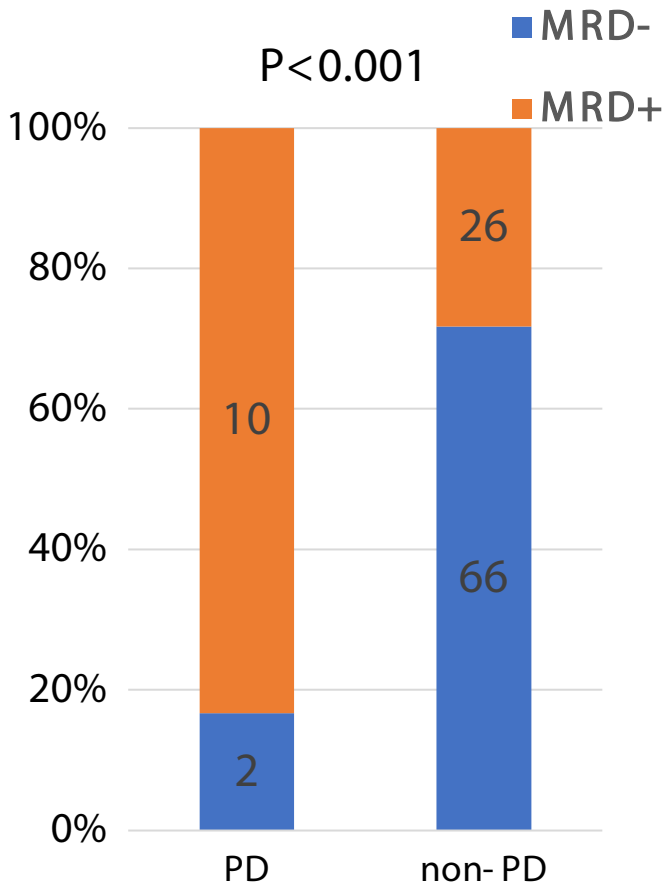
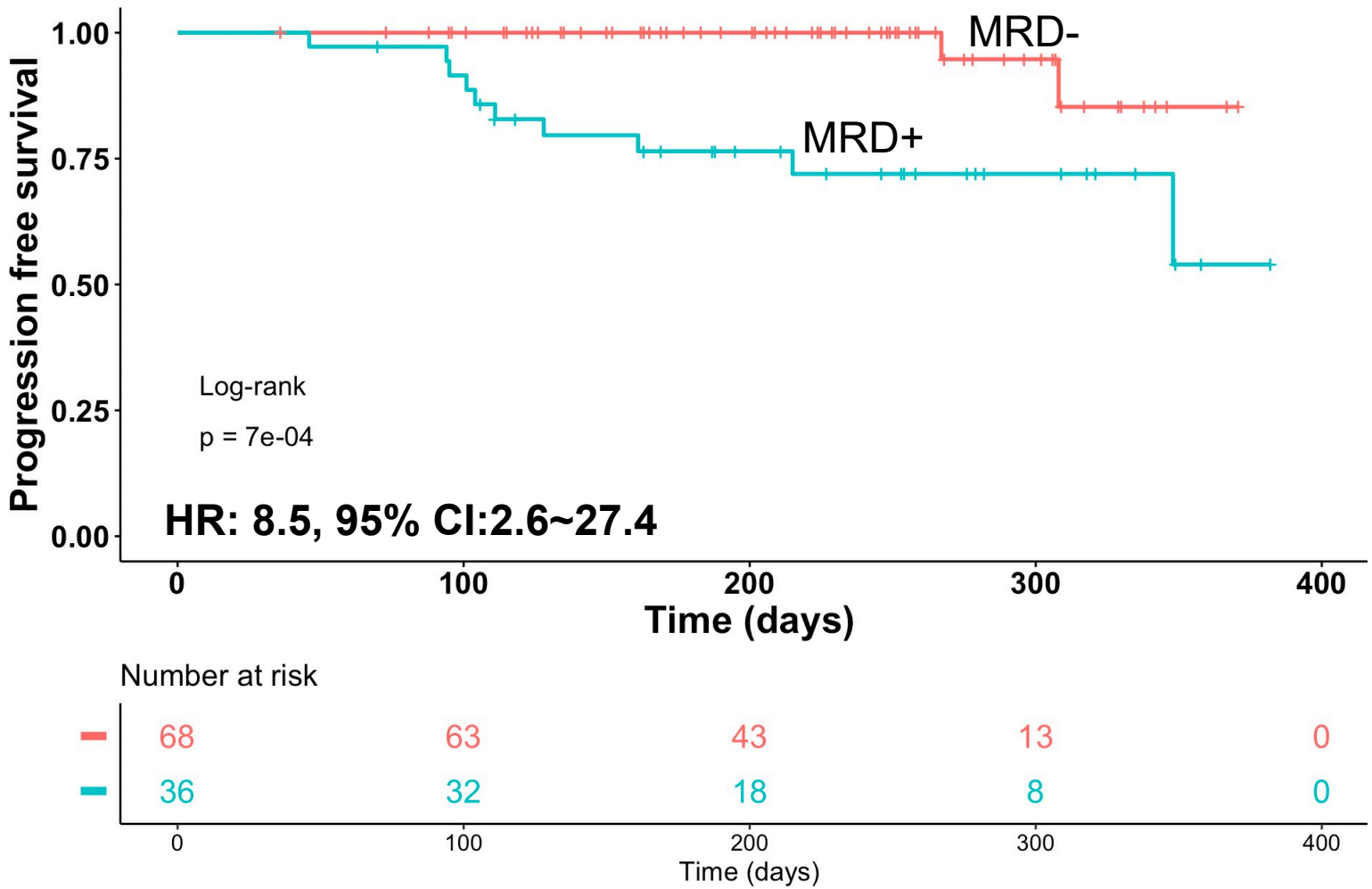
SeekInClarity™ analysis at landmark

MRD status at landmark is prognostic on treatment effectiveness





*Samples collected after 2 cycles were defined as landmark, except 4 out of 104 patients used 1 cycle samples instead.

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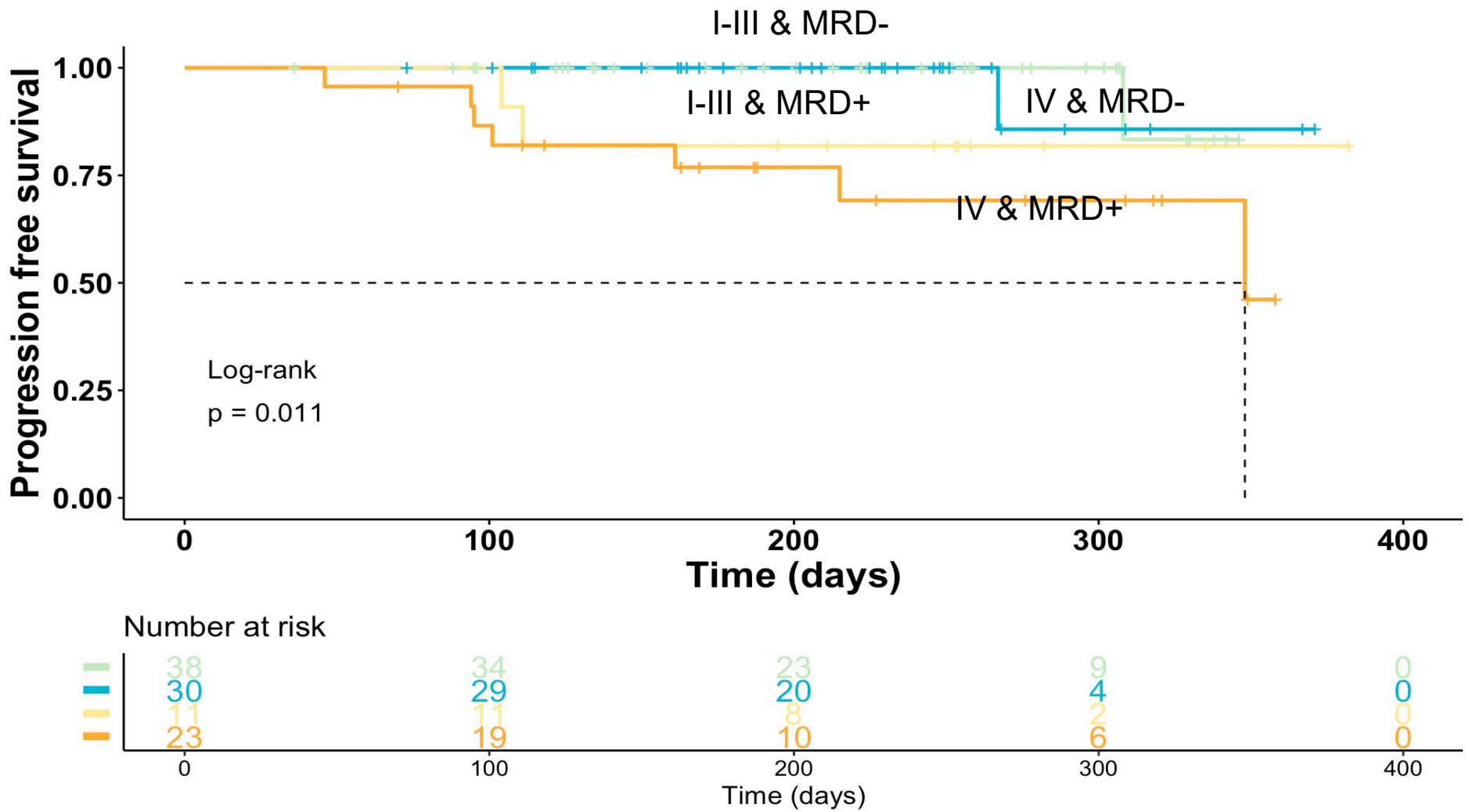
SeekInClarity™ vs tumor stage

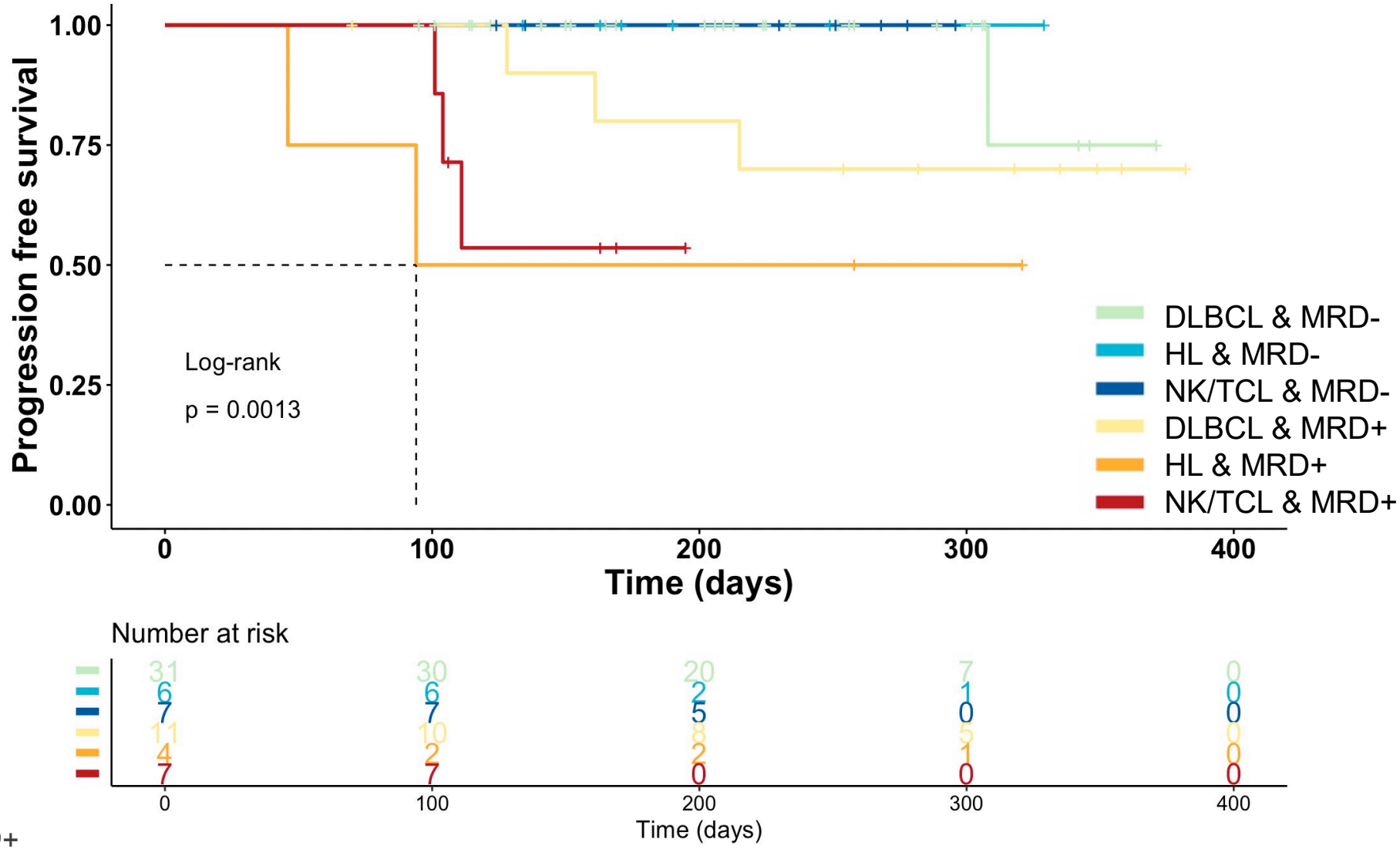
MRD status is more prognostic than tumor staging



Blue: MRD-
Orange: MRD+

SeekInClarity ™ vs different subtypes

MRD status is more prognostic than lymphoma subtyping

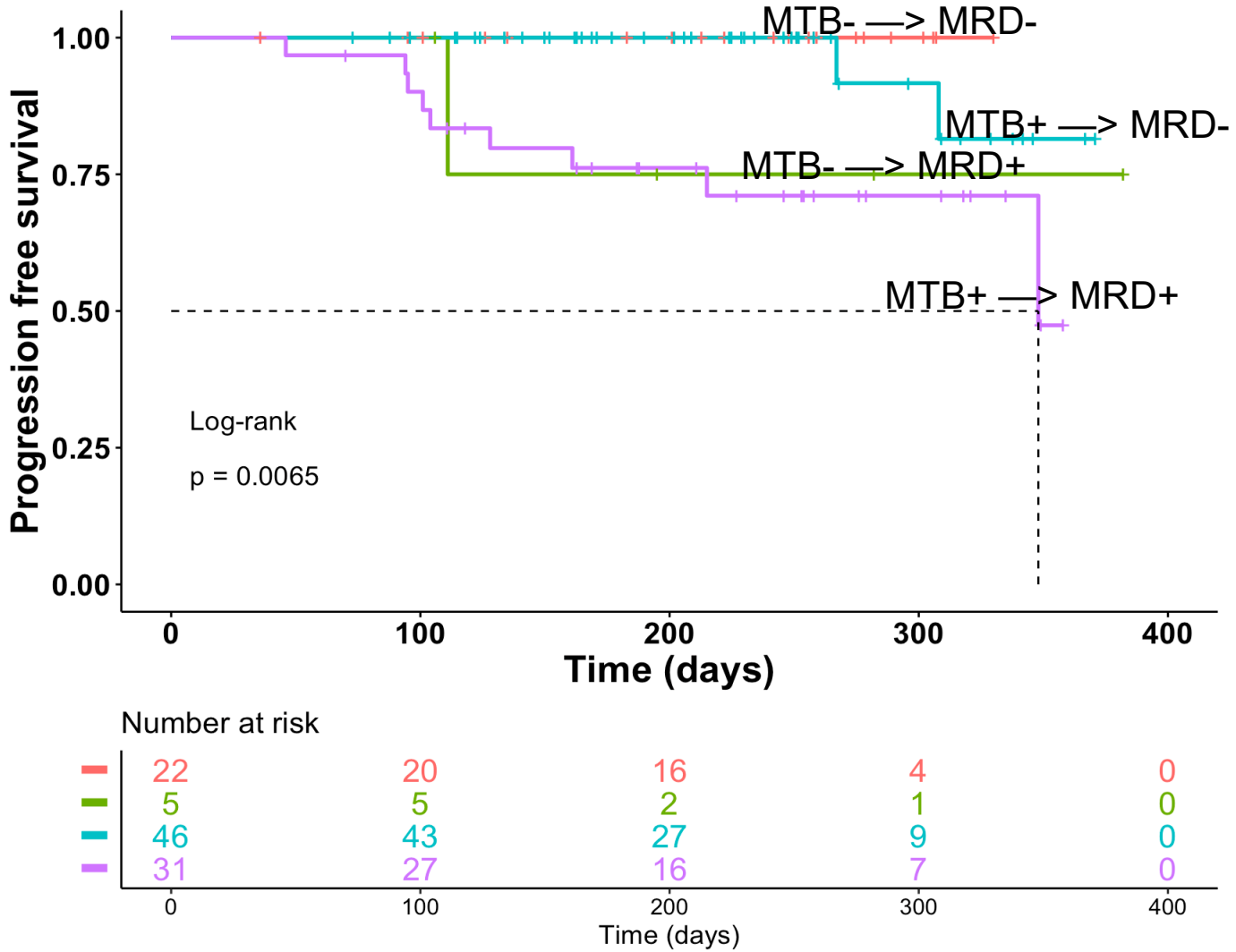


Blue: MRD-
Orange: MRD+

MTB status changes before/after treatment

Patients who are MTB negative at both before and after treatment do extremely well

Baseline —> landmark



60% TMB+ (baseline) patients can achieve MRD- (ctDNA/PTM clearance) at Landmark

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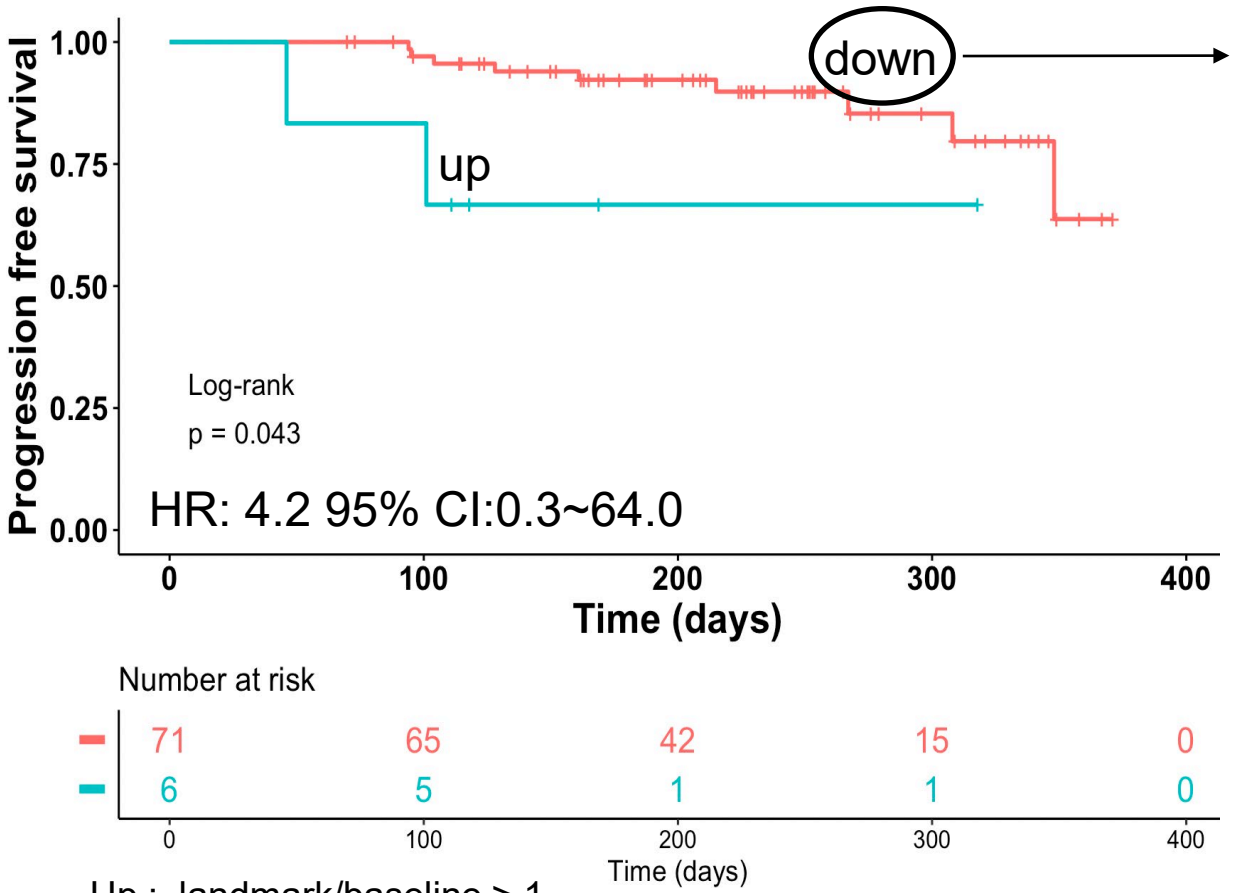
MTB dynamic changes before and after treatment

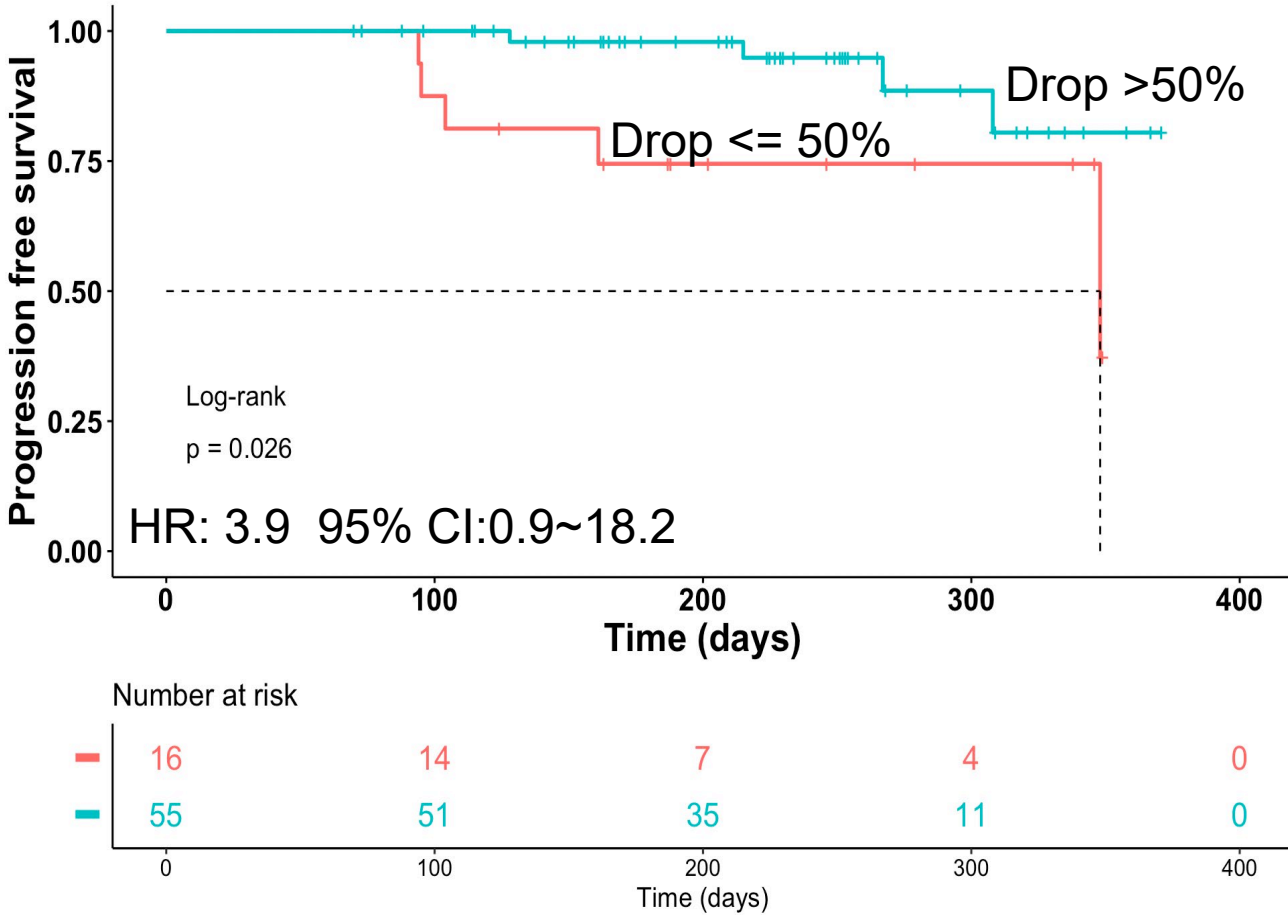
MTB dynamic change and the rate of MTB/ctDNA clearance are correlated with outcome

MTB dynamic changes in baseline + group



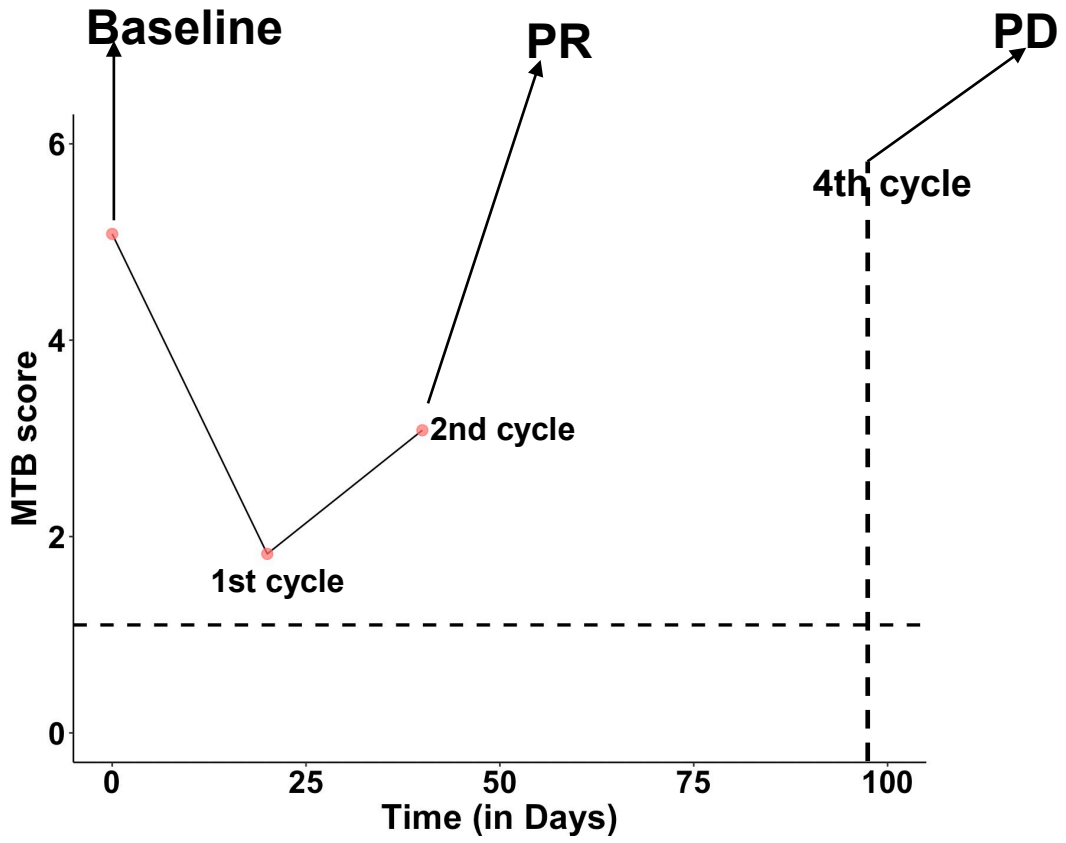
Up : landmark/baseline > 1
Down: landmark/baseline < 1

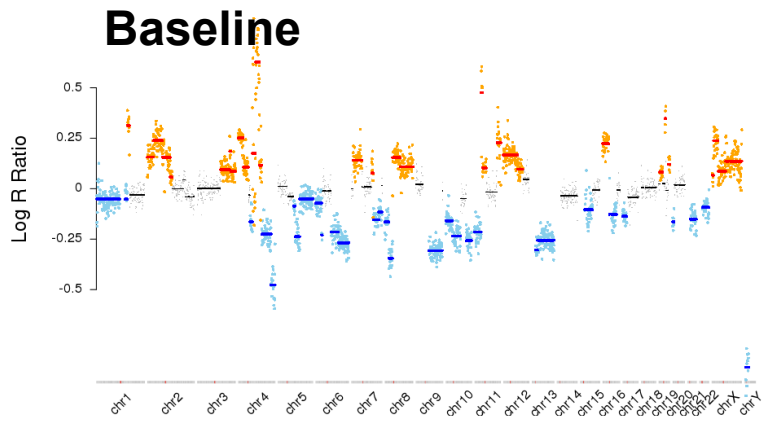
MTB dynamic changes in baseline + and down group

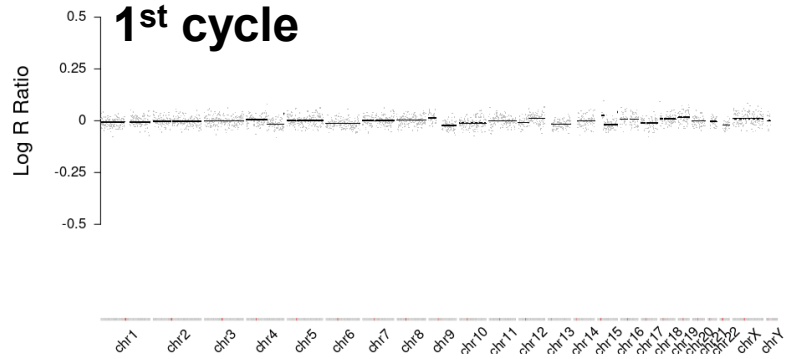


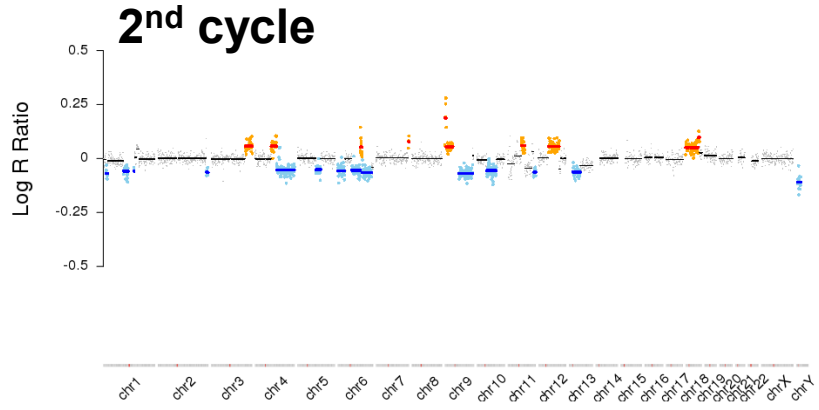
SeekInClarity™ (demo case)

Dynamic change of MTB is prior to imaging (CT) change



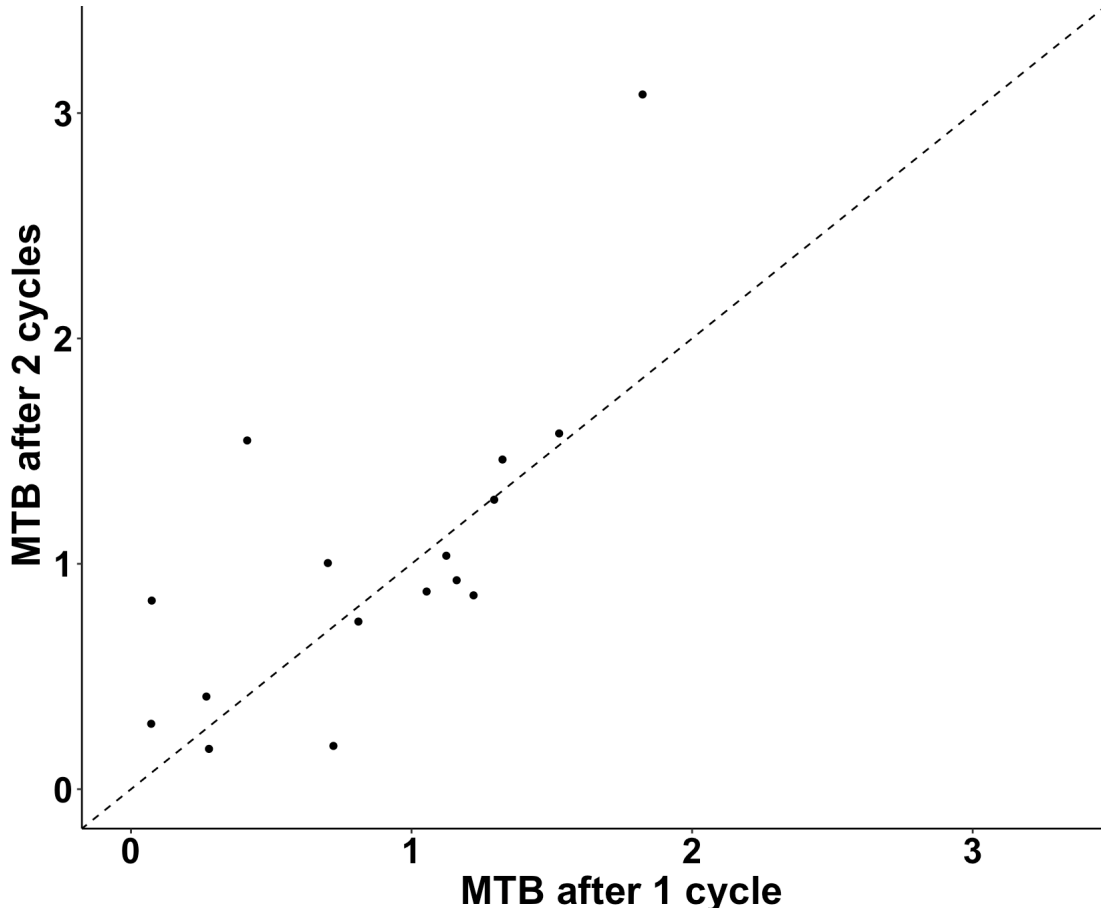


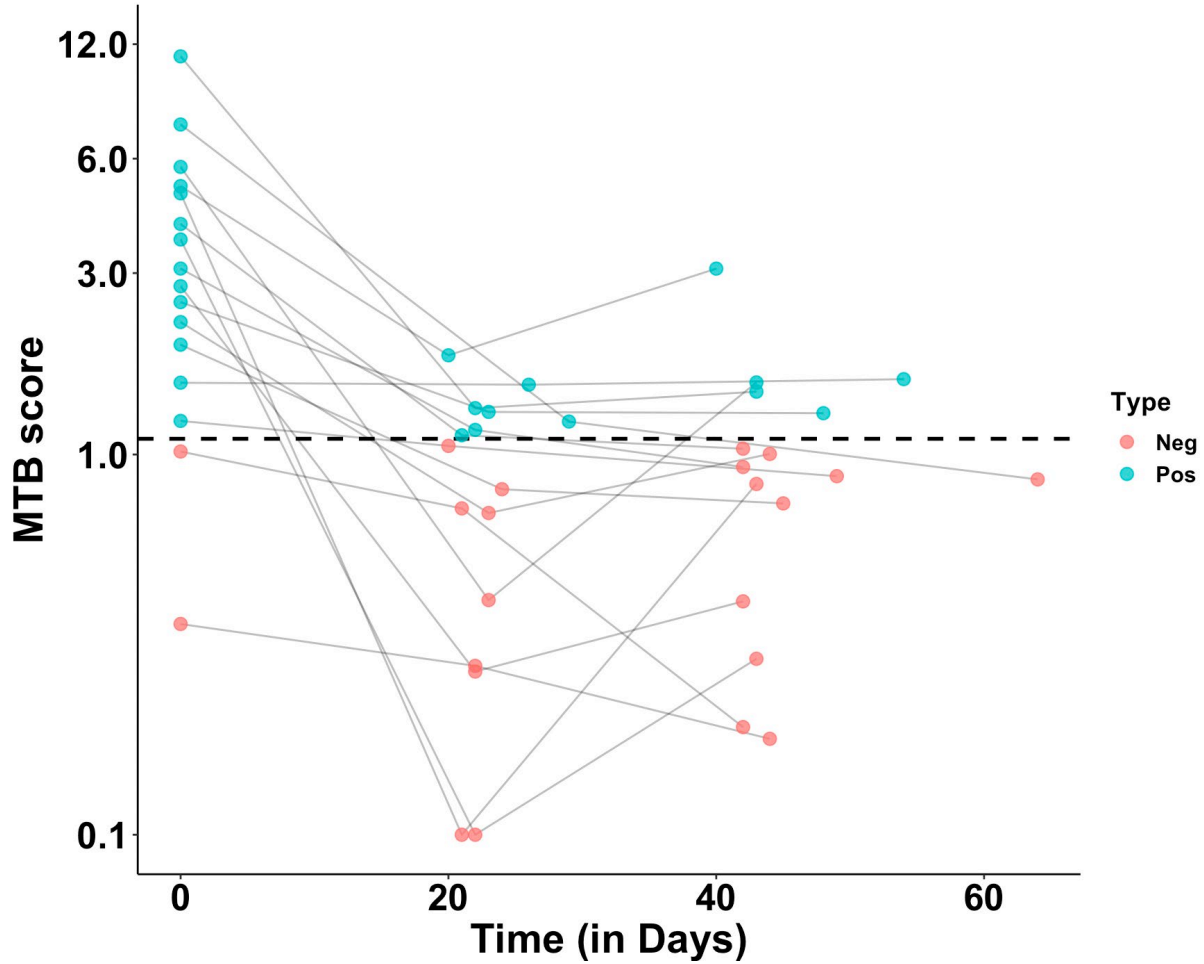




MTB: 1 vs 2 cycles of treatment

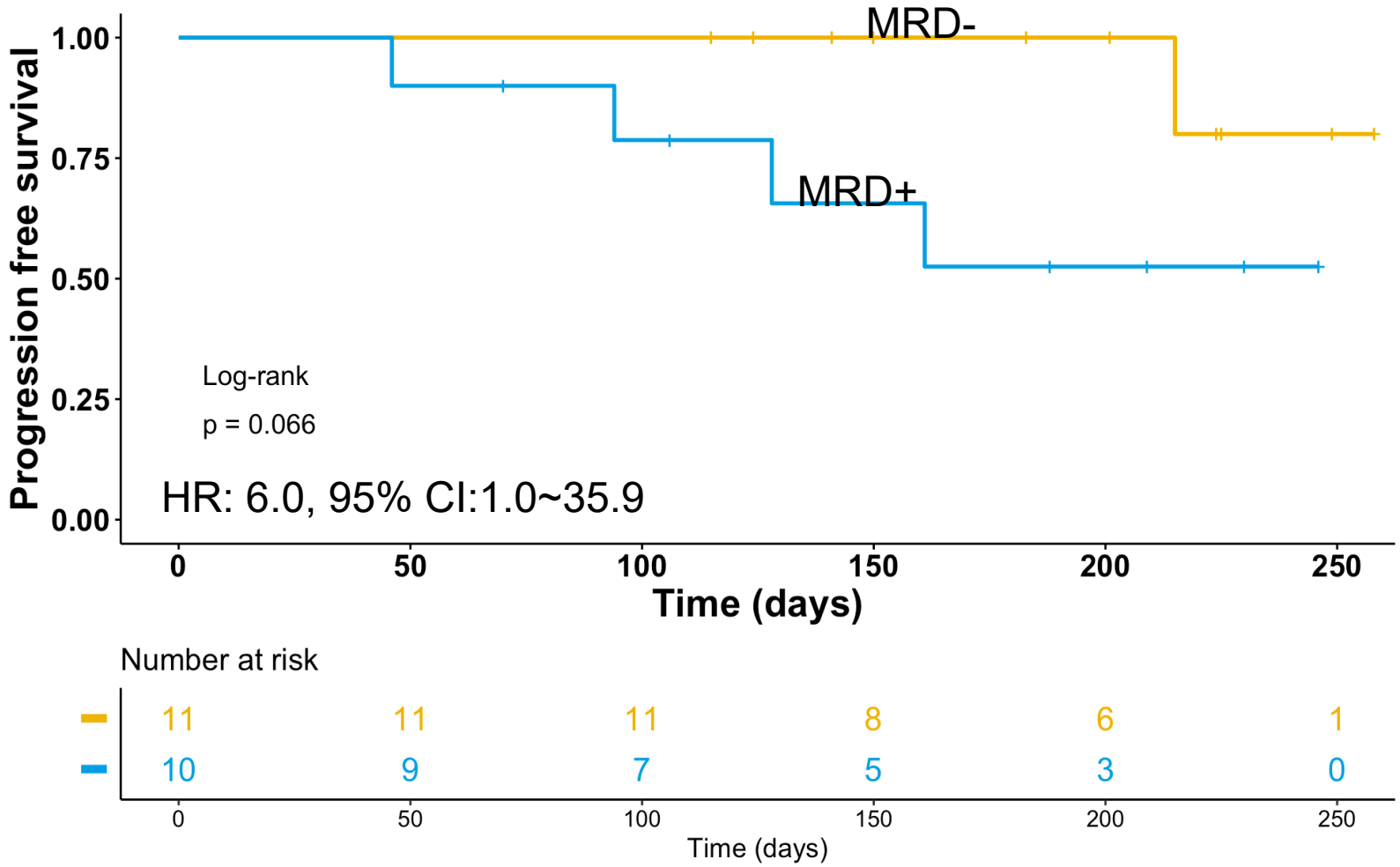
MTB value after 1 cycle treatment has a good concordance with that after 2 cycles treatment





MRD statue after one cycle treatment is sufficient to predict outcome

Even only after one cycle treatment, SeekInClarity also has prognostic value for therapeutic effectiveness



Quick and quantitative assessment of efficacy is the holy grail of oncology drug clinical development

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SeekInClarity™ – summary

- SeekInClarity is a cost-effective pan cancer/pan indication treatment response monitoring test that does not require cancer tissue analysis.
- Both baseline MTB and landmark MRD values are prognostic.
- Double negative (MTB- and MRD-) patients have a very favorable outcome (100% PFS).
- Double positive (MTB+ and MRD+) patients have the worst outcome.
- 60% baseline positive patients can achieve ctDNA/PTM clearance (MRD-) after 2 cycles of treatment.
- SeekInClarity analysis after 1 cycle of treatment is sufficient to assess response.

Blood tests for getting right treatments at earlier time

Advancing equitable cancer care through innovation

	思康宁® SeekIn Care® Pan-cancer early detection	SeekIn Cure™ 思康安® Pan-cancer Recurrence monitoring	SeekInClarity™ Pan-cancer Treatment Response monitoring 思康明®
Indicated subjects:	Healthy population	Post-op patients of radical resection	Late-stage patients
Launch date:	Nov. 2018	May 2019	Aug. 2020

One-Size-Fits-All

SEEKIN & INSPIRE2LIVE
GROUND-BREAKING NEW TECHNOLOGY FOR MULTI-CANCER EARLY DETECTION
JOINING FORCES FOR THE BENEFIT OF PATIENTS
#WeAreThePatientsVoiceInCancer
#IfAboutUsNotWithoutUs

Lead the World!

真理至上，以人为本

seek and you will find

– Matthew 7:7

SeekInCare® - Comparison to other cancer early detection tests

	Method	Sensitivity	Specificity	Pan-cancer	Tissue of origin
Plasma tumor markers	chemiluminescence、 flow cytometry based fluorescent microsphere...	30%	92%	✓	✓ (<20%)
Specialized cancer detection	varied based on different cancer types	varied based on different cancer types and technologies. Mainly applied for high-risk individuals.		✗	✗
Grail Multi-cancer	cfDNA methylation	51.5%	99%	✓	✓ (89%)
SeekInCare ® Pan-cancer	cfDNA CNA & FS Plus PTMs	68%	98%	✓	✓ (67%)

Comparison with other common technical approaches

Company	Technical methodology	Enrichment	Sequencing	Cost	Genomic coverage	Sensitivity	Specificity
Grail	cfDNA methylation panel	Targeted capture probes	139X NGS	NA	1 M methylation sites	51.5% [1]	99% [1]
Thrive	ctDNA mutation Targeted capture panel[4]	Targeted capture probes /Multiplex PCR based amplicons	3000X NGS	$ 500	10-1000 genes	70% [2]	99% [2]
Delfi	cfDNA fragmentomics	In silico enrichment of cancer signals (Fragmenomics)	2X WGS	NA	Whole genome (3 B bases)	73% [3]	98% [3]
SeekIn	cfDNA panoramic view + Protein tumor markers	In silico enrichment of cancer signals (CNA and FS)	3X WGS	$ 200	Whole genome (3 B bases)	75% [4]	99% [4]

1. Liu, M. C. et al. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. Annals of Oncology 31, 745–759 (2020).
2. Cohen, J. D. et al. Detection and localization of surgically resectable cancers with a multi-analyte blood test. Science 359, 926–930 (2018).
3. Cristiano, S. et al. Genome-wide cell-free DNA fragmentation in patients with cancer. Nature, 570(7761):385-389. (2019).
4. Mao, M. et al. Development of a blood-based cancer screening assay with a novel multivariate cancer risk score (MCRS) model by integrating shallow WGS data and plasma protein markers. Oral presentation at ASCO Breakthrough 2019.

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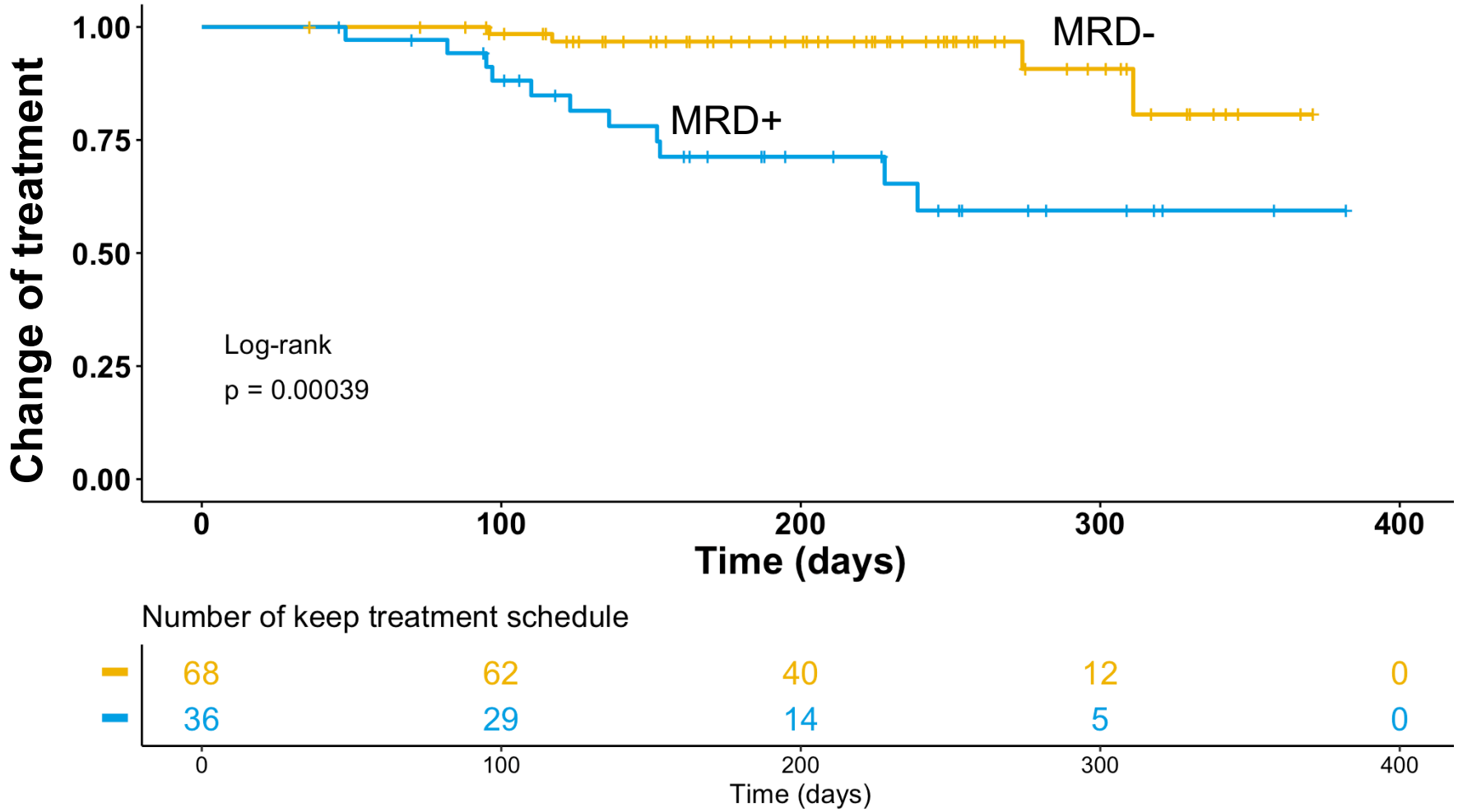
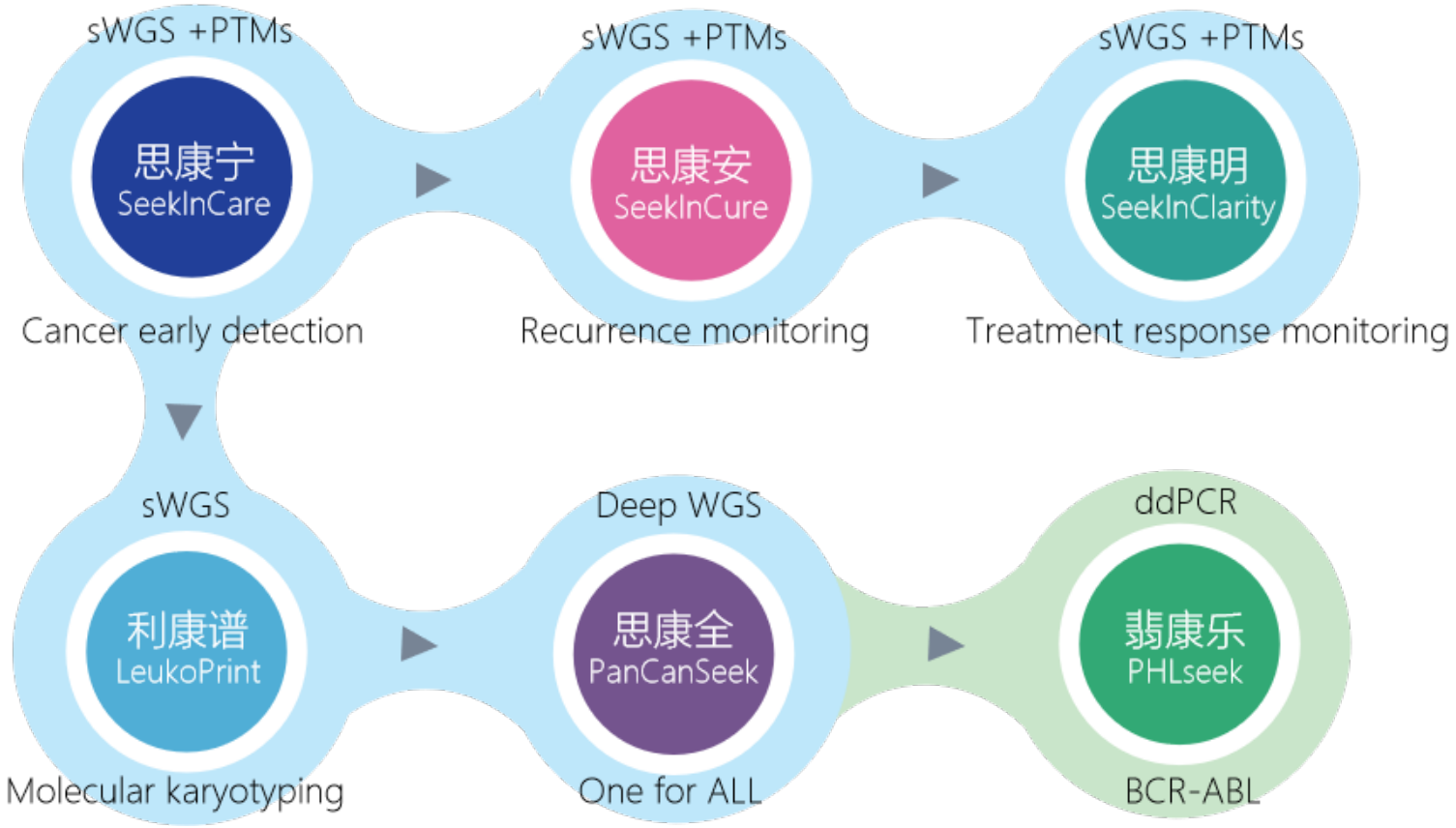
SeekInClarity™ analysis at landmark

Time to changing the first-line treatment in MRD+ group is significant less than that in MRD- group.



From Solid Tumor to Leukemia



LeukoPrint® A new generation of genetic molecular technology

LeukoPrint®
利康谱®®

the first-in-class Leukemia sWGS CNA test

CE Marking

- Without culturing cells in vitro
- High sensitivity and low failure rate
- Automatic readout system

By evaluating the copy number aberration (CNA) in Bone marrow cells and/or circulating cell free DNA (cfDNA) via shallow whole genome sequencing (sWGS), in conjunction with conventional cytogenetics, LeukoPrint® makes leukemia diagnosis, molecular subtyping, prognostic stratification and treatment responds monitoring more precise and comprehensive.

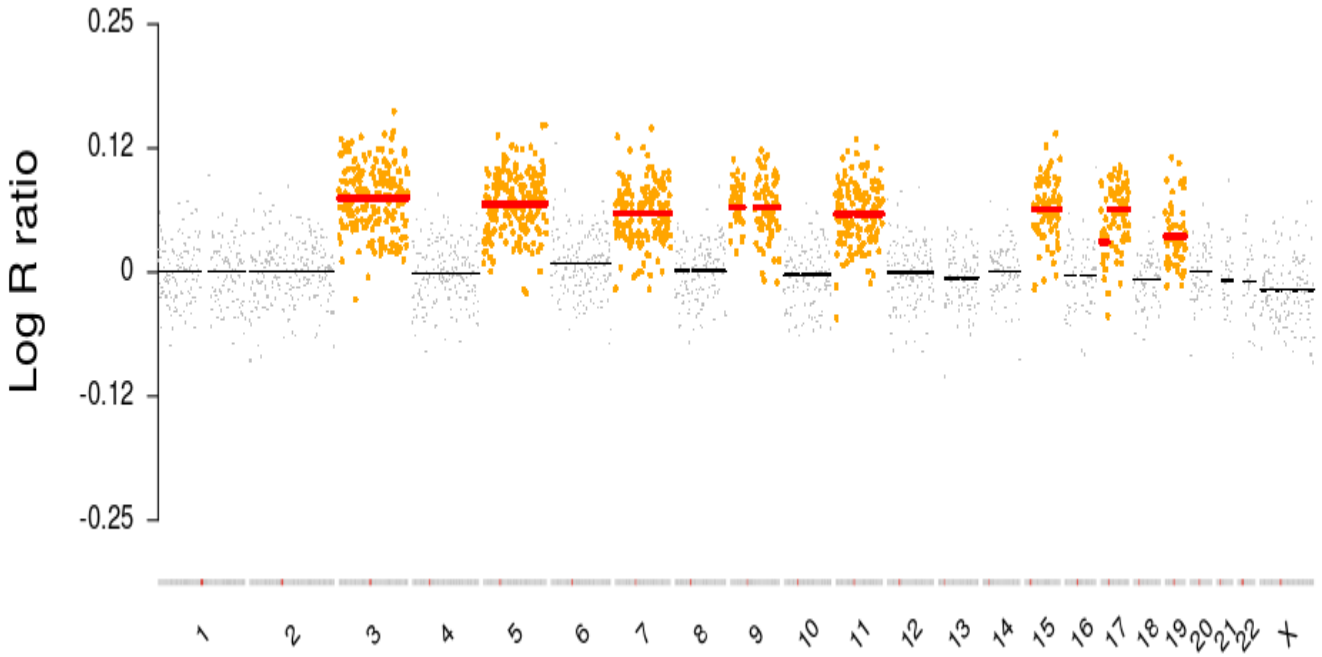
- Sample requirement: 10ml blood
- TAT: 10 work days
- Results readout: copy number aberration (CNA)
- Indicated subjects: Patients with suspected or confirmed leukemia (MDS/AML/ALL/CLL/MM)

Comparison to other karyotyping tests

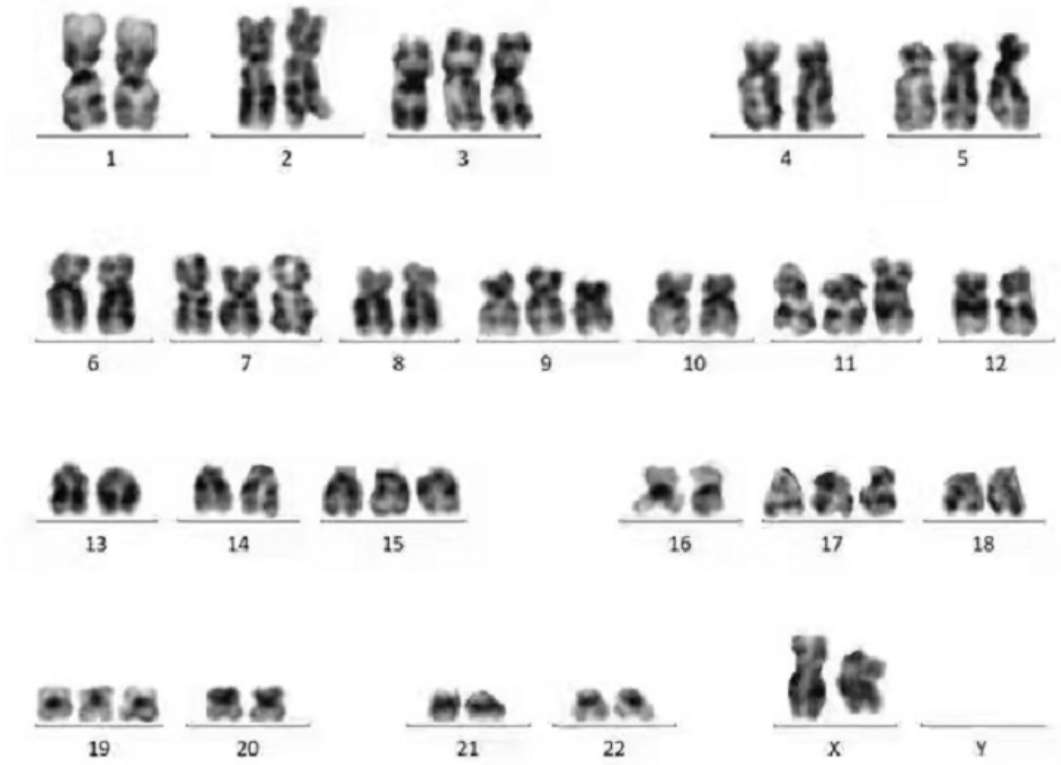
	Karyotyping	FISH	LeukoPrint®
Coverage area	23 pairs of chromosomes	Sigle probe	Whole genome
Resolution	≥5Mb	≥100kb	≥100kb
Sample Requirement	High	High	Low
Readout	Visual inspection	Visual inspection	Digital
Throughput	Low	Low	High
TAT	7-10d	3-5d	10-12d
Cost	Medium	High	Medium

Figure 2

A



B



染色体位置标注出来

PanCanSeek® Integrated Solutions of Cytogenetics and Molecular Diagnosis in Leukemia

PanCanSeek®

思康全®

CE Marking

One for All

01

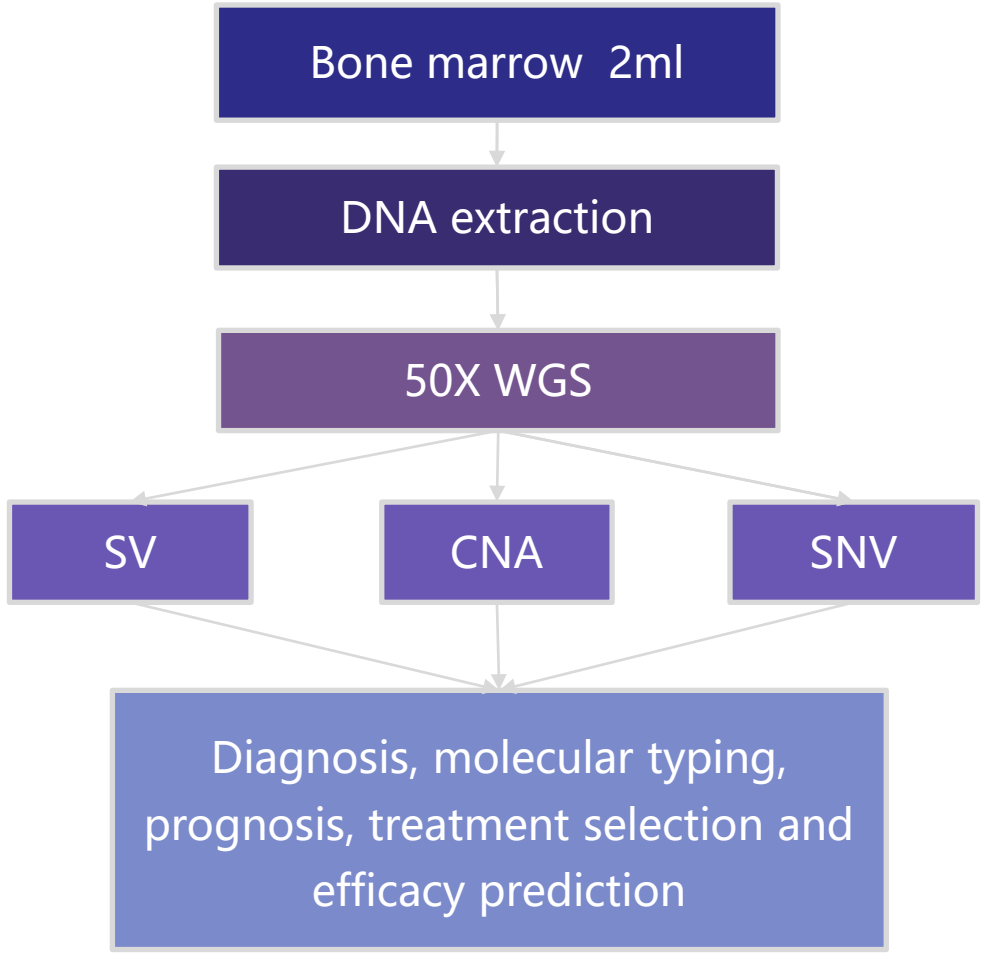
Structural variants (SV)

02

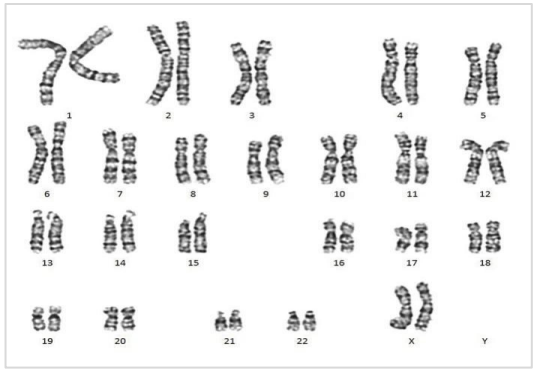
Copy number variation (CNA)

03

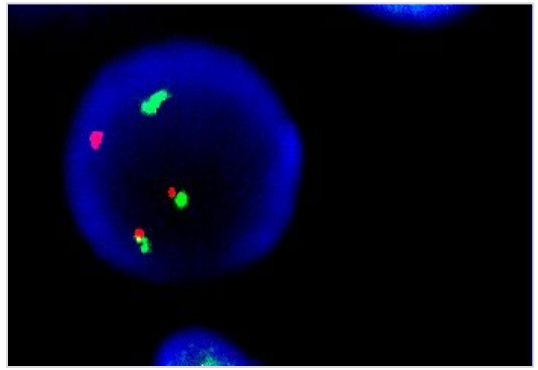
Point mutations (SNV, INDEL)



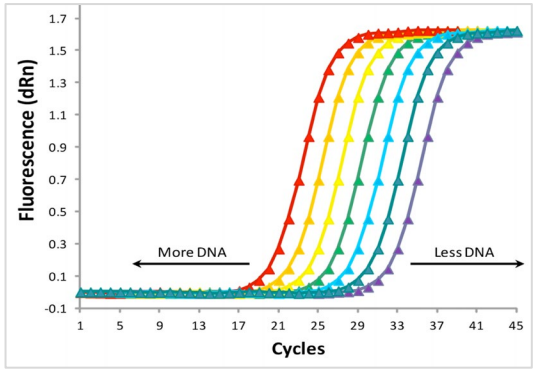
PanCanSeek® faster, more accurate and more comprehensive



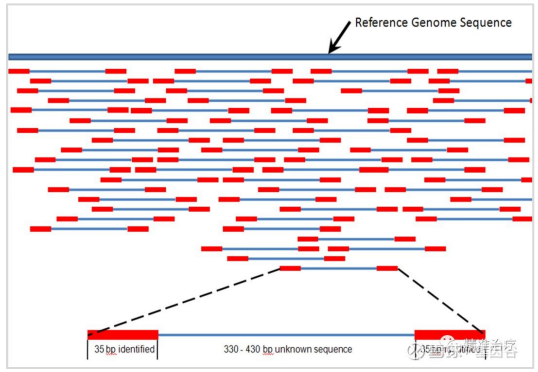
Karyotyping



FISH

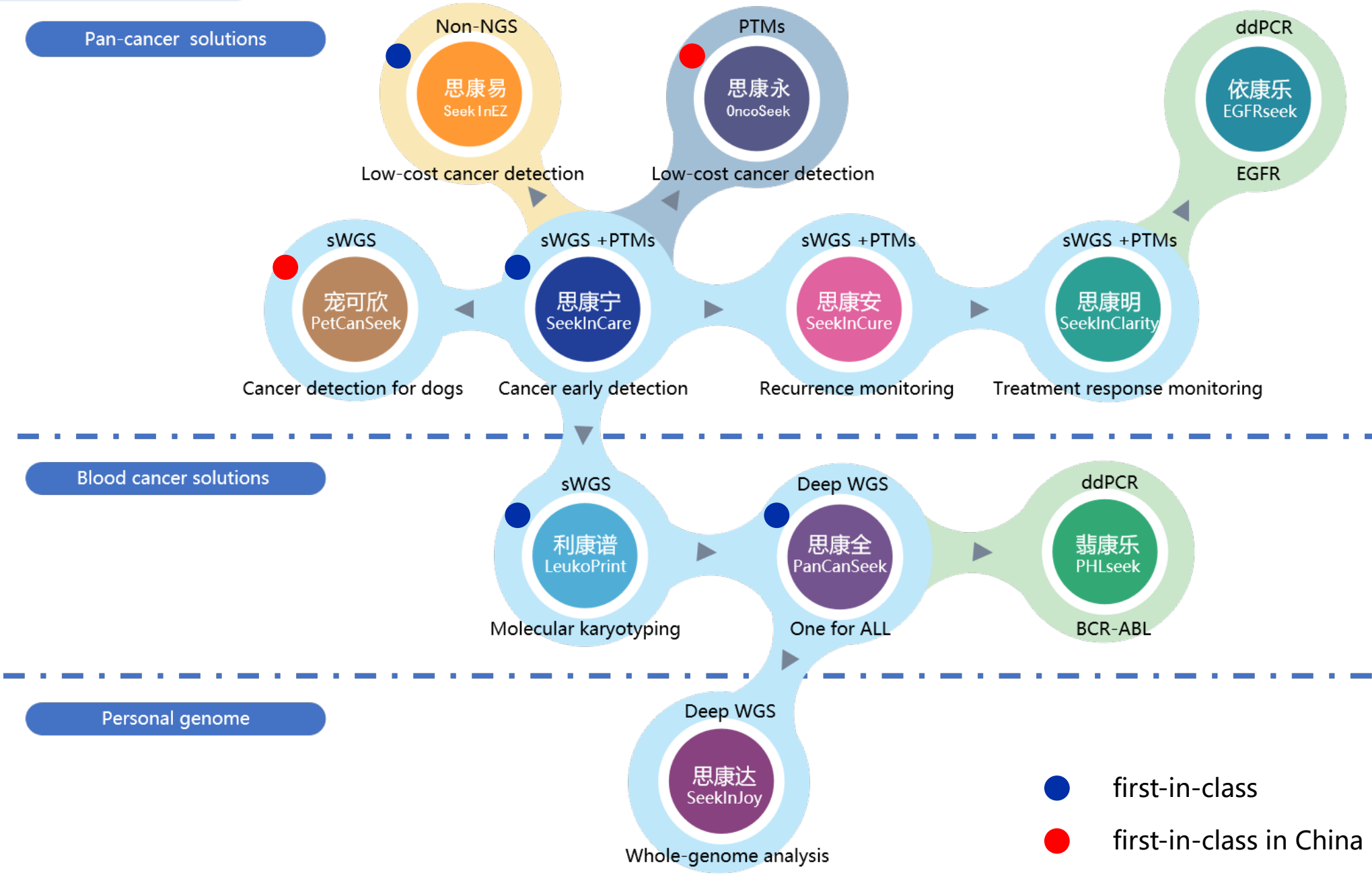


qPCR



NGS Panel

思康全®PanCanSeek®

Compared with traditional diagnostic methods, PanCanSeek can complete the detection of all genetic mutations in leukemia patients in one single test - faster, more accurate and more comprehensive

Product portfolio