Irish On Line Molecular Tumour Board

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cancer trials ireland

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

ESMO
Designated Centres of Integrated Oncology and Palliative Care

BON SECOURS HEALTH SYSTEM

ctg
UCC CANCER TRIALS GROUP

Disclosures

- Paid Speaker for Foundation Medicine Internal Training
- Roche Ireland Research Grant, Advisory Boards and Conference Travel
- Conference Travel – Merck, Ipsen, Astra Zeneca
- Advisory Boards – Pfizer, MSD, Merck, Ipsen, Astra Zeneca, Servier, Leo
- Consulting; Servier Ireland

Irish Healthcare – brief background

- Population just over 5 million people
- Universal Public Care provided by HSE – good for trauma and severe illness, can have delays in diagnosis and treatment of other conditions
- Some delays of reimbursement for cancer drugs in public sector
- 50% pay for private health insurance – now cover any intravenous EMA approved anti cancer therapy in private hospitals only
- Some of the insurance companies will pay for one NGS test per year – usually Foundation Medicine

Cancer in Ireland

An estimated

44,000 new cases

including:

3,941 prostate

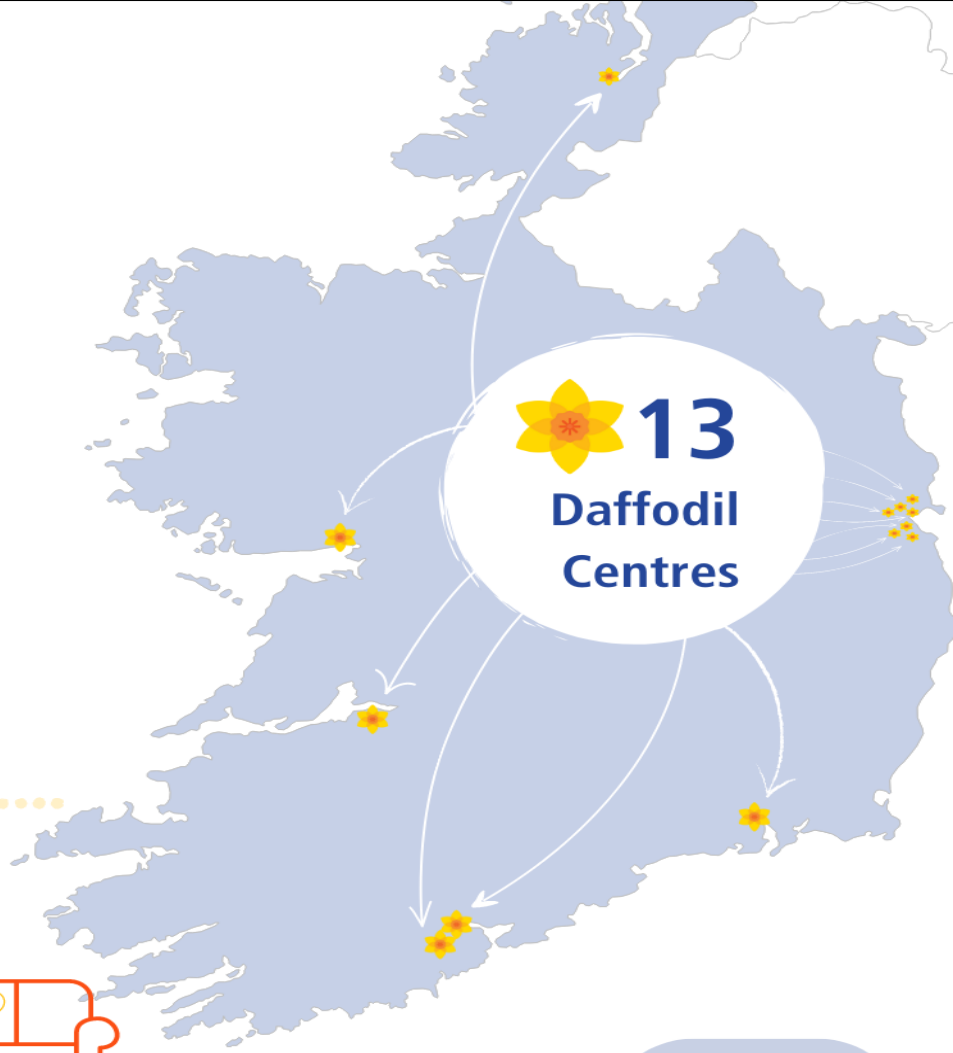
3,392 breast

2,672 lung

2,562 bowel

12,668 skin

Based on National Cancer Registry Ireland (NCRI) statistics 2018–2020



The impact of your support in 2022

22,388
people helped by our Support Line and Daffodil Centre nurses

13,035
trips by volunteer drivers to take patients to treatment

7,323
nights of Night Nursing for patients to spend their final days at home

22,388
counselling sessions provided by our services in-person and remotely

Irish Cancer Society

Support Line
Freephone
1800 200 700

My practice

- **Light or never smokers** – 1/3 of my lung cancer patients have a drugable mutation
- **Educated patients** – ask for cutting edge treatments
- **Willing to self fund NGS tests** – Guardant, Foundation, Natera
- **Occasionally willing to self fund drugs** (e.g. Enhertu, Nivolumab)
- **Fantastic Hospital Pharmacy** – lots of compassionate access drugs e.g. Adagrasib, TDM1, Atezolizumab, Pemigatinib
- **Active Clinical Trials Unit** – preferred option always

Life used to be simple

- 15 years ago I started in full time private practice
- Lung Cancer – EGFR, ALK
- Oesophageal Cancer – Her2
- Colorectal Cancer – MSI, MMR, RAS/RAF
- Lymphoma – GCB vs non GCB

Oncomine™ Focus Assay Gene List

Hotspot genes, n=35

AKT1
ALK
AR
BRAF
CDK4
CTNNB1
DDR2
EGFR
ERBB2
ERBB3
ERBB4
ESR1
FGFR2
FGFR3
GNA11
GNAQ
HRAS
IDH1
IDH2
JAK1
JAK2
JAK3
KIT
KRAS
MAP2K1
MAP2K2
MET
MTOR
NRAS
PDGFRA
PIK3CA
RAF1
RET
ROS1
SMO

Copy Number Variants, n=19

ALK
AR
BRAF
CCND1
CDK4
CDK6
EGFR
ERBB2
FGFR1
FGFR2
FGFR3
FGFR4
KIT
KRAS
MET
MYC
MYCN
PDGFRA
PIK3CA

Fusion drivers, n=23

ALK
RET
ROS1
NTRK1
NTRK2
NTRK3
FGFR1
FGFR2
FGFR3
MET
BRAF
RAF1
ERG
ETV1
ETV4
ETV5
ABL1
AKT3
AXL
EGFR
ERBB2
PDGFRA
PPARG

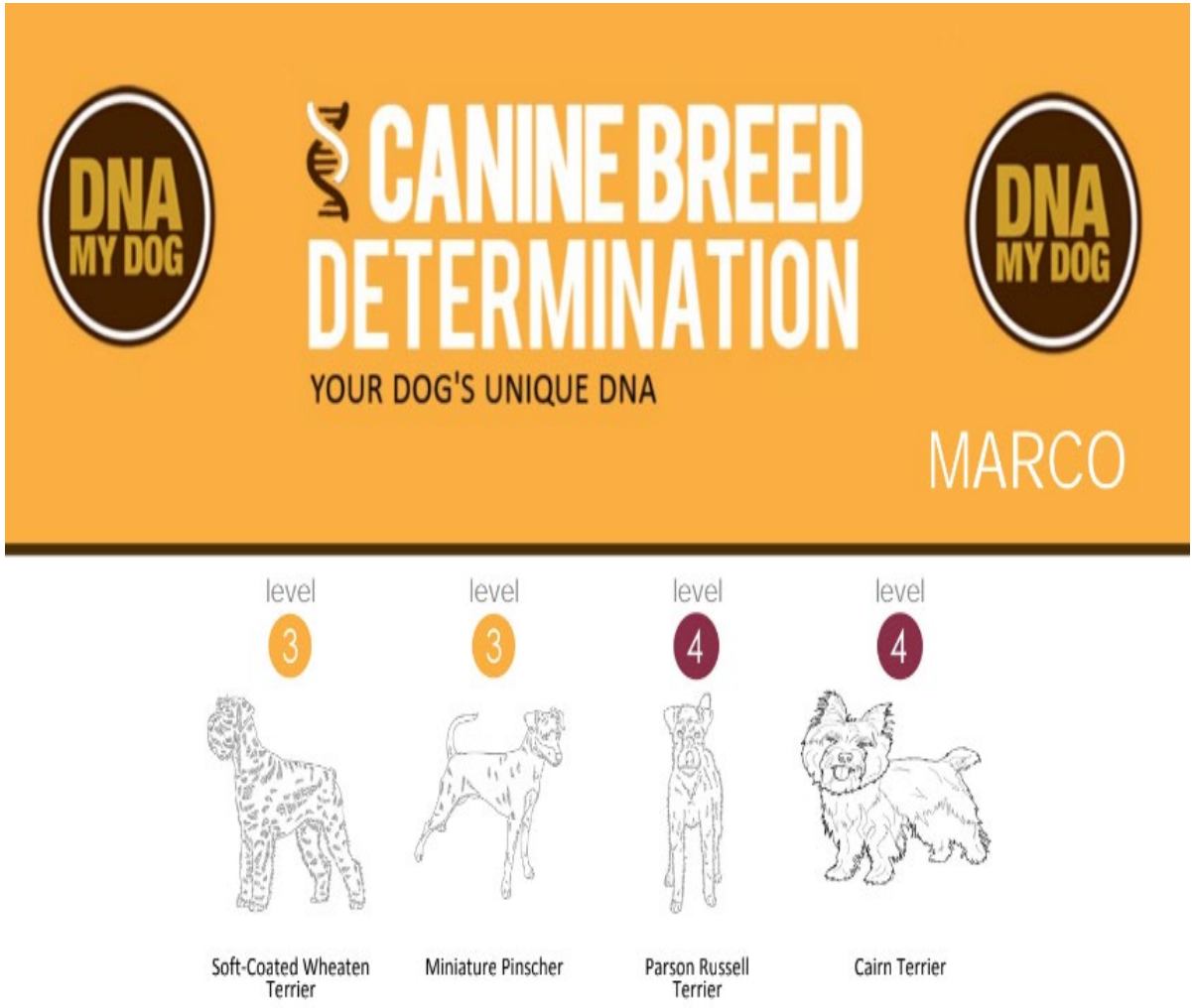
DNA Panel

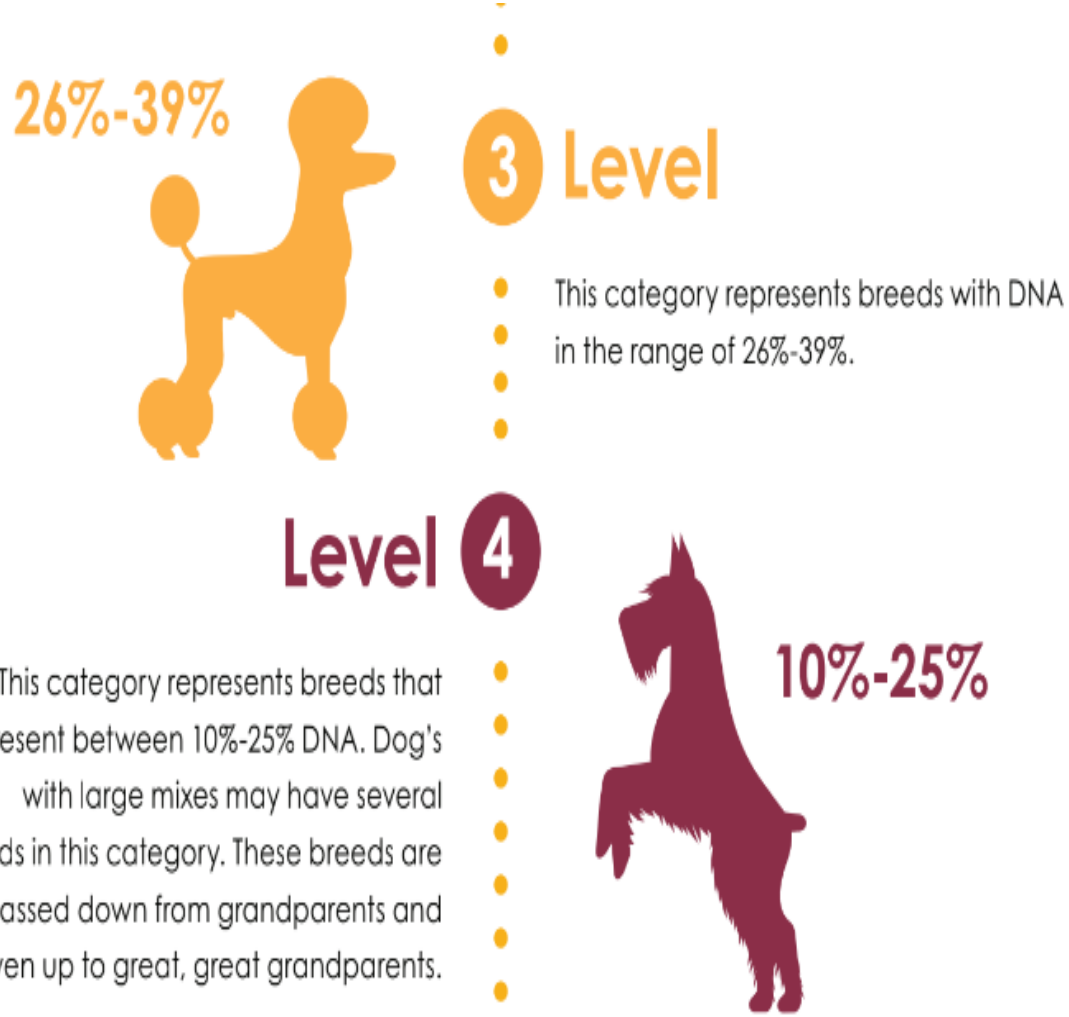
RNA Panel

Life is now complicated

- Lung Adeno Carcinoma
  - basic molecular panel of 10 mutations and fusions (Oncomine)
  - PDL1 Tumour Proportion Score
  - Tissue NGS / ctDNA especially if progressing on TKI

GENOTYPE


DNA MY DOG
CANINE BREED DETERMINATION
YOUR DOG'S UNIQUE DNA
DNA MY DOG
MARCO
level 3
Soft-Coated Wheaten Terrier
level 3
Miniature Pinscher
level 4
Parson Russell Terrier
level 4
Cairn Terrier


26%-39%
3 Level
This category represents breeds with DNA in the range of 26%-39%.
Level 4
This category represents breeds that represent between 10%-25% DNA. Dog's with large mixes may have several breeds in this category. These breeds are passed down from grandparents and even up to great, great grandparents.
10%-25%

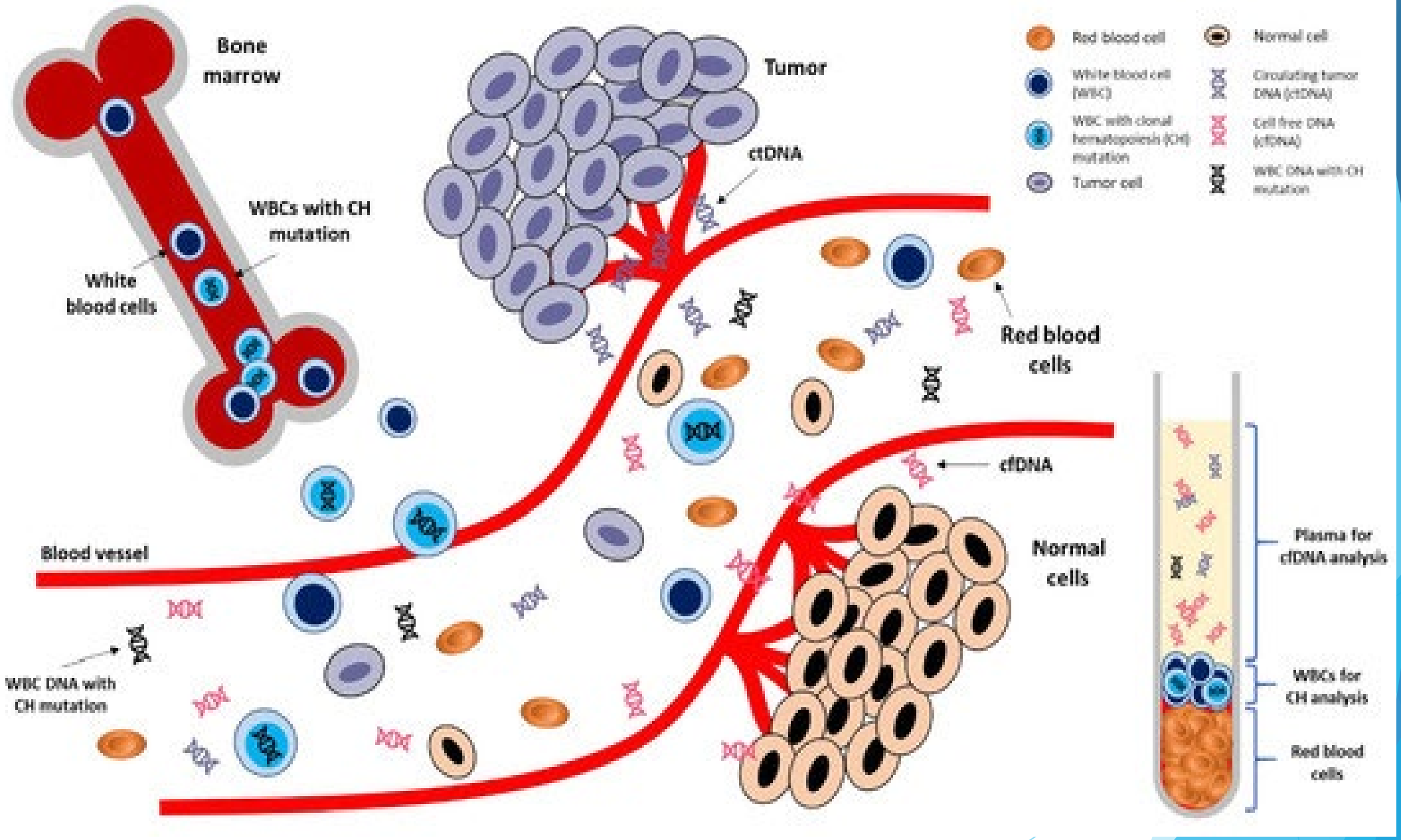
PHENOTYPE

Pitfalls for the Clinician who orders NGS

- CHIP
- Hereditary Cancer Syndromes
- Non targetable mutations
- Insufficient DNA shed from tumour into blood
- Low Variant Allele Frequency (<1%)
- Non availability of targeted therapies even with strong clinical data

Barriers to NGS

- Funding
- Availability of Drug
- Fear of mis interpreting data



BEWARE OF CLONAL HAEMATOPOIESIS in liquid biopsies

How can a busy clinician cope with modern precision data?

- Experience
- Reading the Literature
- Molecular Tumour Boards

Role of the MTB

- MTB empowers clinicians to make educationally informed drug treatment decisions through discussion
- MTB enhances understanding of NGS interpretation including genetic implications
- MTB may help with the decision on appropriate treatment choices
- All the above leads to increased patient benefits and outcomes

National On Line MTB

- Set up through Ms. Deirdre Poretti in Roche and Dr Dearbhaile Collins
- Arms length funding from Roche to Accenture who originally ran on line meetings
- Panel of Irish and International Experts commenting on 1-3 anonymized cases in 1 hour
- Now organized by Cancer Trials Ireland with pan industry support
- Responsibility rests with prescribing physician (me) but anonymized report of MTB generated – useful for seeking compassionate access drugs and documentation

Format of the MTB session

- Monthly 1 hour virtual sessions
- 3 cases discussed from hospitals nationally
- 4 attending experts sharing insights
- National invited discussants pertinent to cases
- Cases submitted ~1.5 weeks prior to MTB

Anonymized patient information shared on patient case template

NGS results are shared in a structured way so that experts can prepare the patient case and HCPs can have an informed discussion during a MTB session

Key questions are submitted to the experts prior to the MTB session

Experts

Rodrigo Dienstmann, M.D., PhD, MBA - Medical Oncology

- Principal Investigator of the Oncology Data Science Group of the Vall d'Hebron Institute of Oncology (VHIO) in Barcelona, Spain.
- Medical Director of Oncoclínicas Precision Medicine, São Paulo, Brazil.

Stephen Finn, MB BAO BCh FDS PhD FRCPath FFPATH - Pathology and Cancer Genomics

- Associate Professor, Consultant Pathologist and Principal Investigator at The University of Dublin, Trinity College and at St. James's Hospital Dublin.

Marie-Dominique Galibert, PharmD, PhD - Cancer Genetics

- Deputy Director of the Institute of Genetics and Development of Rennes (IGDR), France.
- Head of the Gene Expression and Oncogenesis Research Team – Labellisée Fondation ARC.
- Head of the Department of Molecular Genetics and Genomics and the Co-Director of the FHU-CAMIn (Hospital University Federation - Cancer Microenvironment Innovation) at the Rennes University Hospital.

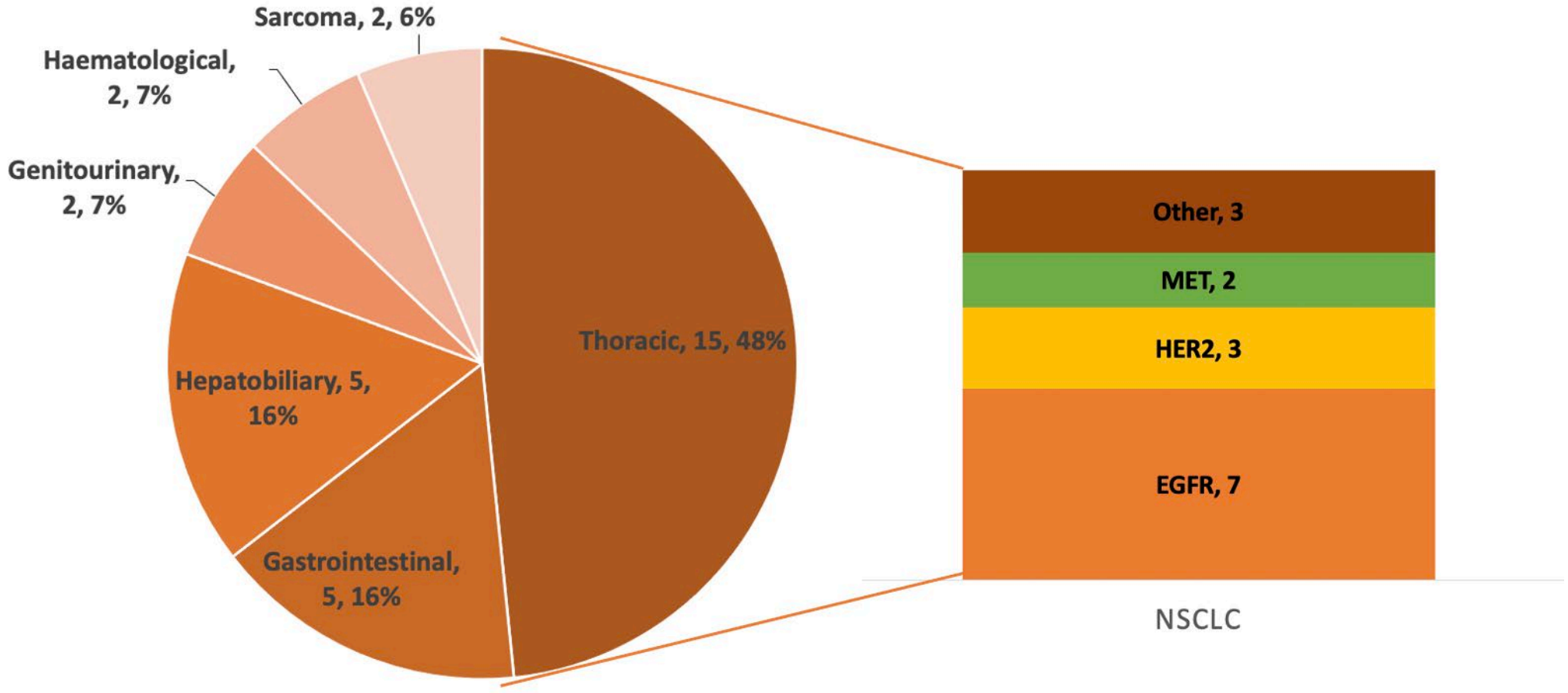
Terri McVeigh, MB BAO BCh (Hons), PGCert. (Med. Gen.), PGDip. (Med. Sci.), MSc. (Clin. Ed.), PhD, MRCP, MRCS - Cancer Genetics

- Consultant clinical geneticist in the Royal Marsden NHS Foundation Trust, UK, specializing in cancer genetics.
- Clinical Lead for Postgraduate Certificate in Genetics & Genomics with RCPI.
- Co-Chair of the Health Education England GEP GeNotes Oncogenomics and Malignant Haematology working groups.

What have I learnt from MTB?

- When a new mutation is likely to be actionable e.g. MET alteration in EGFR mutated lung cancer progressing on Osimertinib
- Not to treat CHIP as a drugable target – e.g. ctDNA of a KIT mutation in an EGFR mutated lung cancer progressing on Osimertinib
- When a mutation is interesting but not actionable – PIK3CA in non-breast cancers
- When to refer for Hereditary Cancer Genetics – ATM and MUTYH germline mutation detected in lung cancer patients
- The power of orthogonal testing – do HER 2 IHC to confirm ctDNA detected increased HER2 copy number

MTB Experience May 2022 – June 2023



On Line MTB – evolves over time

- Provides guidance for practicing clinicians to develop expertise in ordering and interpreting NGS
- Helps avoid errors
- May help access to trials and to compassionate access drugs
- As experience grows the complexity of cases chosen for discussion increases and the sophistication of the audience increases
- Clinicians happy to exchange experience with rare diseases and unusual drug toxicities

Industry collaboration: benefits from the MTB program

R&D

Foster drug development and translational research

- Identify **novel therapeutic targets** and **biomarkers**
- **Research** and **clinical trial** involvement/opportunities
- Shape and acquire **new technologies**
- Opportunity for the introduction of **digital technologies** to support precision medicine

Market Access

Increase access of drugs

- Increased local understanding of the **different status of drug availability** in Ireland
- Increased **use of RWD in Ireland** to understand of clinical significance and incidence/prevalence of biomarkers
- Potential alternative access pathway for **orphan drugs/niche targeted therapies** in rare disease/mutation subtypes

Medical

Educate and strengthen relationships

- Increase **physicians experience** with novel compounds and understanding of clinical significance of biomarkers
- Facilitate patient enrollment in **clinical trials**
- Facilitate patients from trials and “named patient programmes” access to **compassionate drug access programmes**

An Actual MTB Case – discussed 3 times over 2 years

Metastatic Colorectal Cancer RAS/RAF wildtype, MMR intact

Post Progression on anti EGFR mAB Guardant 360 showed elevated HER2 copy number

MTB recommended HER2 IHC – strongly positive – MTB recommendation helped get Trastuzumab and Pertuzumab

Progressed through Compassionate Access Trastuzumab Pertuzumab after 3 months – rediscussed – TDxd recommended

Progressed through self pay Trastuzumab Deruxtecan after initial response 4.5 months on treatment

Dr Brian Bird Stage IV Colon Cancer – 3rd MTB discussion September 2023

Patient Case History

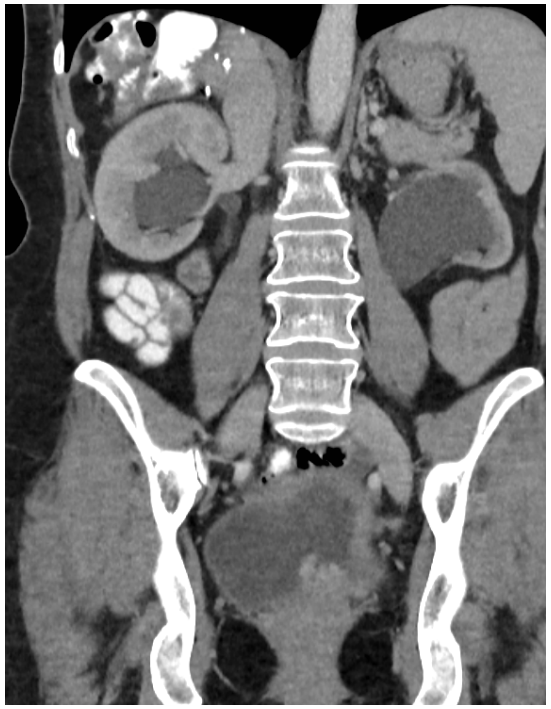
General Description	
Gender	*female*
Age range	*50-55*
Cancer Type and stage	*colon cancer, stage IV*
Tumour cellularity	
DNA/RNA yield	
Test type	*Liquid → Solid*
About the test	*Guardant 360 -> Foundation Med*
Date of test	*1 July 2020 → 19 July 2023*

Patient / Treatment History

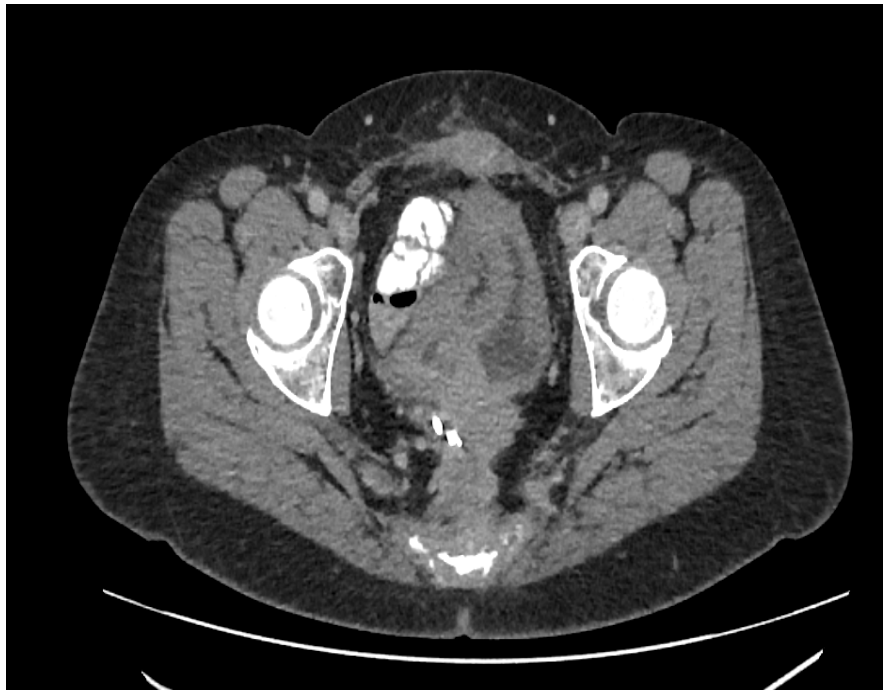
- 52 year old female Laparoscopic LAR for pT4aN2b (13/26 LN+) low sigmoid cancer 20cm. 21/10/16. MMR intact by IHC. RAS/RAF wildtype.
- Imaging revealed a synchronous single liver met – resected followed by 8 x Xelox. Less than 1 year later small lung met resected.
- Multiple mets 2019- FOLFIRI Panitumumab (skin tox ++) 12/07/2019 omentectomy and en-bloc resection of rectum, abdominal hysterectomy and BSO Dec 2019 – back on FOLFIR, XRT to abdo wall nodules.
- **4 cycles of Trastuzumab and Pertuzumab completed Jan 2021 – PD**
- Stable disease on Irinotecan Bev until Sept 22, brief course of TAS-102 (LONSURF)
- Multifocal Progression in lungs and abdomen
- **Self Pay Enhertu (TDxd) Feb – June 2023 – Initial SD after 3 cycles then PD post C6 Repeat bladder biopsy still strongly HER2+ by IHC – Foundation Med test ordered**
- Palliative XRT to new pre sacral mass
- Back on Capecitabine and Bevacizumab

Dr Brian Bird Stage IV Colon Cancer

Additional information



CT SCAN pre cystoscopy and resection of bladder mass Sept 22



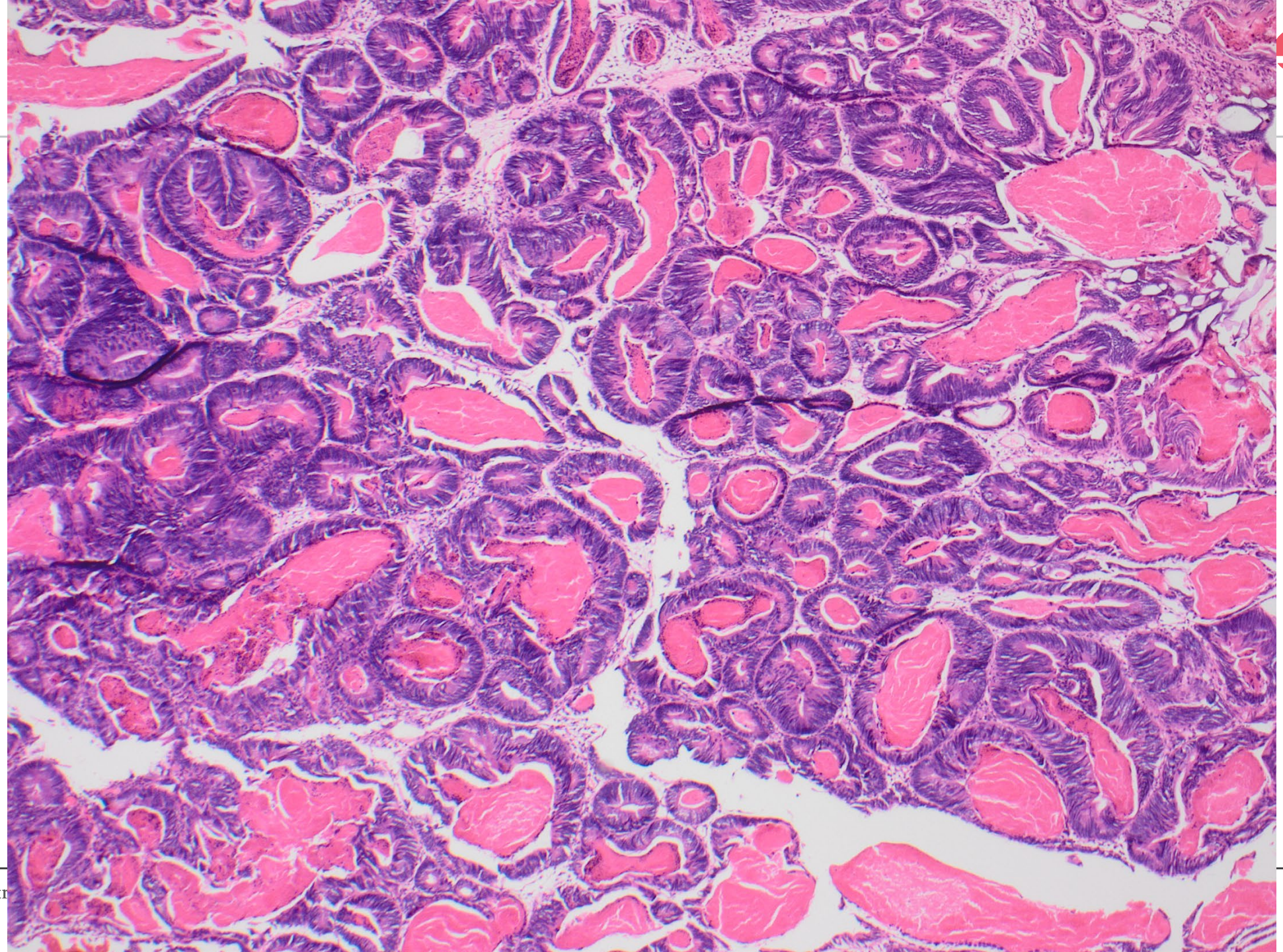
CT SCAN POST ENHERTU – enlarging destructive presacral mass

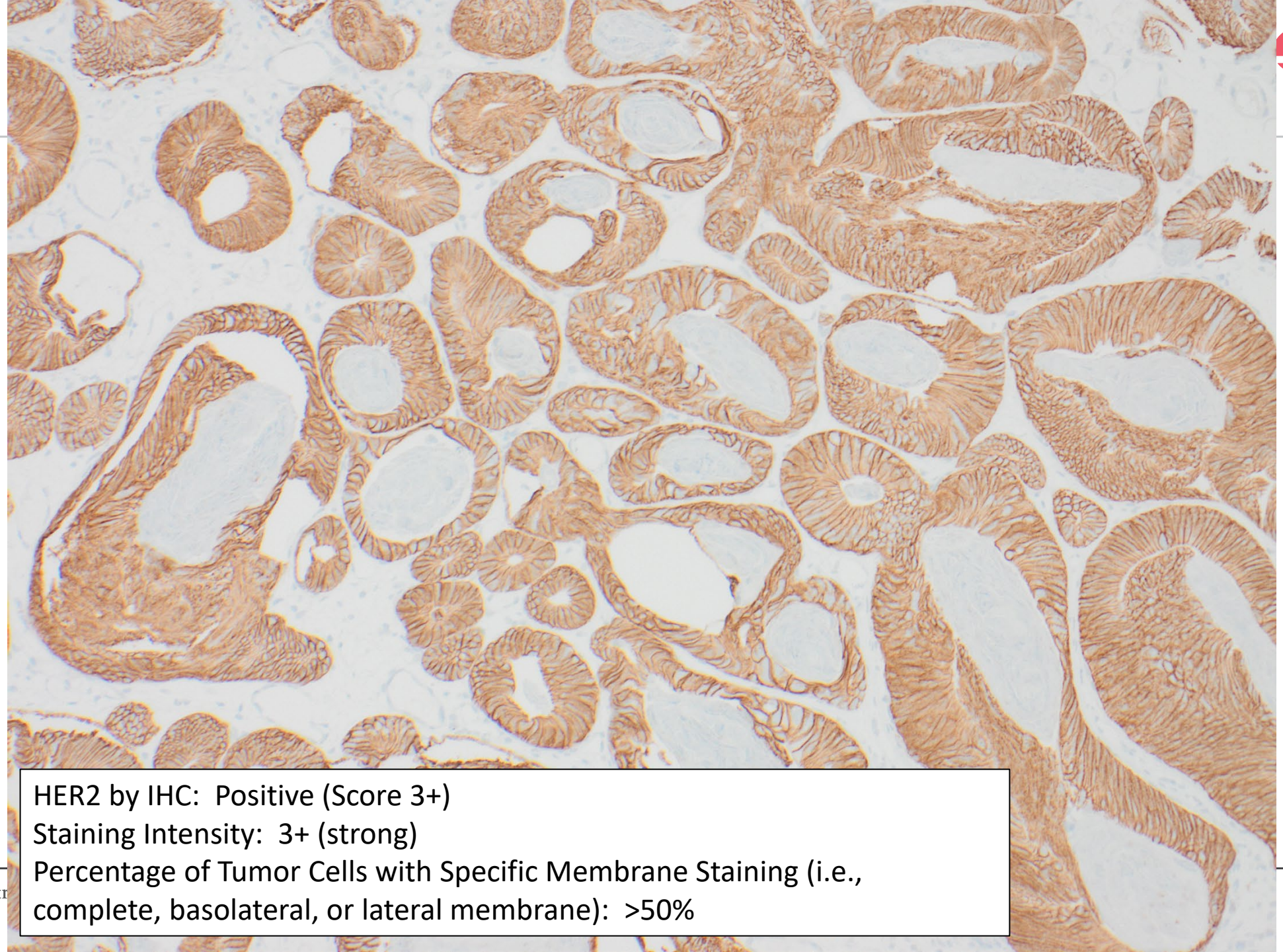
Dr Brian Bird Stage IV Colon Cancer

Initial Biomarker and Genomic Findings

Genomic Findings from G360 1 July 2020					
Finding Name	*MSI - high*	Finding Name	***HER2 Amplification***	Finding Name	***TP53 Splice Site SNV***
Finding Details	***Not Detected***	Finding Details	***Medium (++) Plasma Copy Number: 3.2***	Finding Details	***1.4% cfDNA***

Genomic and Immunohistochemistry Findings from Resected Bladder Mass 21 Sept 2022					
Finding Name	***RAS/RAF***				
Finding Details	***WILDTYPE***				
Finding Name	***Her 2 IHC***				
Finding Details	***Strongly positive (3+)***				





HER2 by IHC: Positive (Score 3+)
Staining Intensity: 3+ (strong)
Percentage of Tumor Cells with Specific Membrane Staining (i.e., complete, basolateral, or lateral membrane): >50%

Dr Brian Bird Stage IV Colon Cancer

Repeat Tissue Biomarker and Genomic Findings August 2023

Genomic Signatures

Microsatellite status - MS-Stable
Tumor Mutational Burden - 2 Muts/Mb

Gene Alterations

For a complete list of the genes assayed, please refer to the Appendix.

ERBB2 amplification
KRAS wildtype
NRAS wildtype
MET MET-CAPZA2 non-canonical fusion
CTNNB1 splice site 40_241+24del226
MYC amplification - equivocal†
SMAD4 loss exons 2-8
SOX9 Q375fs*9
TP53 splice site 672+1G>T

3 Disease relevant genes with no reportable alterations: *BRAF, KRAS, NRAS*

† See About the Test in appendix for details.

Report Highlights

- Targeted therapies with **NCCN categories of evidence** in this tumor type: **Trastuzumab + Lapatinib** (p. 14), **Trastuzumab + Pertuzumab** (p. 15), **Trastuzumab + Tucatinib** (p. 15), **Trastuzumab deruxtecan** (p. 16)
- Targeted therapies with **potential resistance** based on this patient's genomic findings: **Cetuximab** (p. 11), **Panitumumab** (p. 12)
- Evidence-matched **clinical trial options** based on this patient's genomic findings: (p. 17)

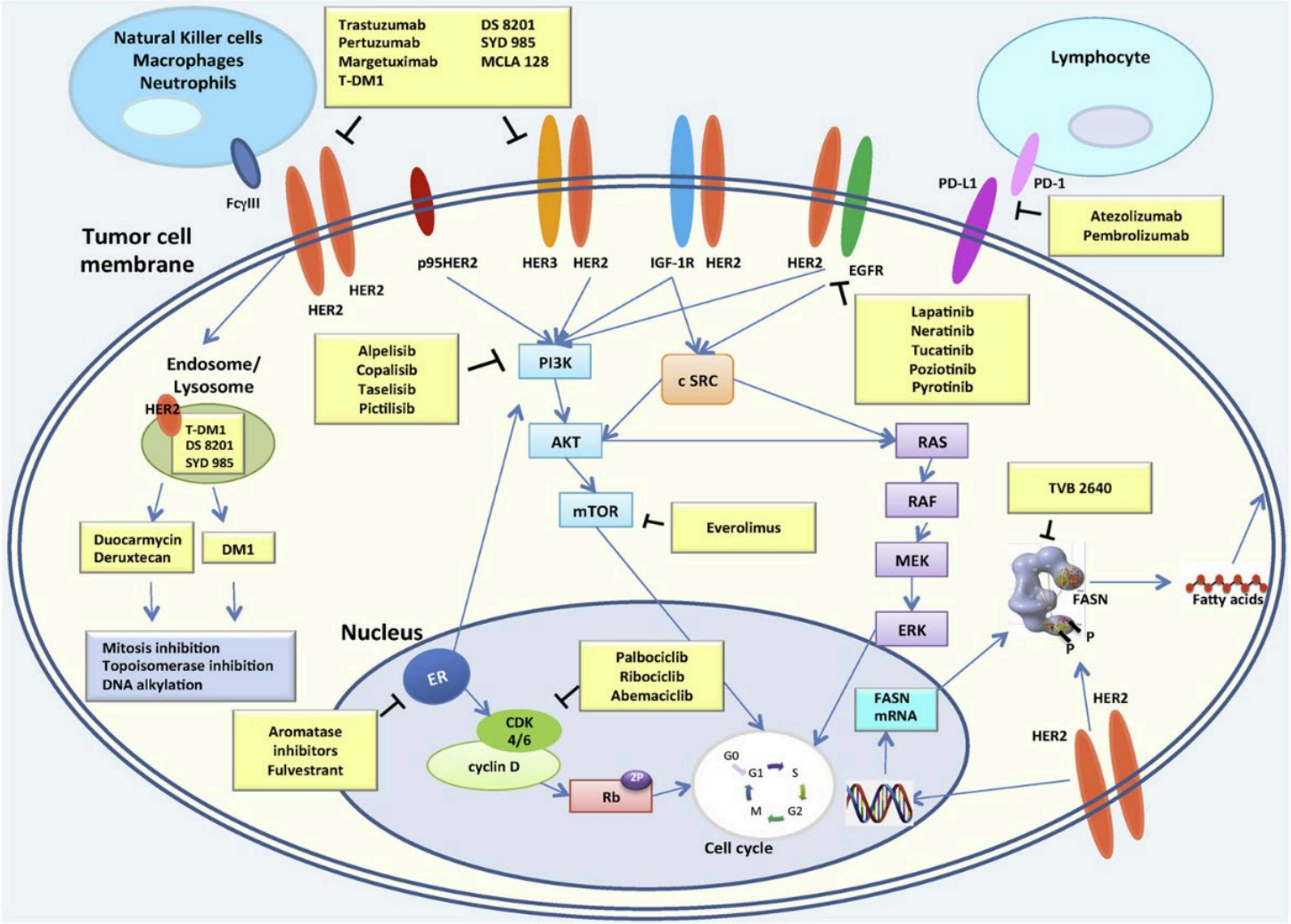
GENOMIC SIGNATURES	THERAPY AND CLINICAL TRIAL IMPLICATIONS
Microsatellite status - MS-Stable	**No therapies or clinical trials.** See Genomic Signatures section
Tumor Mutational Burden - 2 Muts/Mb	**No therapies or clinical trials.** See Genomic Signatures section

Dr Brian Bird Stage IV colon cancer

Key questions

General methodology questions	▪ What is the mechanism of resistance to Trastuzumab Deruxtecan?
Questions tailored to the patient case	▪ Is any other anti HER2 therapy indicated? ▪ Should we consider Fruquintinib if available in future?

Mechanisms of Resistance



C. Vernieri, et al Critical Reviews in Oncology / Hematology 139 (2019) 53–66

Mechanisms of Resistance

Table 1
Mechanisms of resistance to anti-HER2 agents.

Anti HER2 agent(s)	Mechanism of resistance	Factors involved
Trastuzumab (T)	Impaired HER2 binding	Low HER2 levels
	Parallel/downstream pathways	Splicing variants (p95HER2; Δ16 HER2)
	Enhanced lipid metabolism	PI3KCA mutations, PTEN loss
	ER signaling	FASN
	Cell cycle regulation	ER-PgR expression
	Escape from ADCC	Cyclin D1-CDK 4/6 expression
		Poor binding to CD16A
Lapatinib (L)	HER2 signaling	*HER2* mutations
	Cell cycle regulation	Cyclin D1-CDK 4/6 expression
	Parallel/Downstream pathways	PI3K/AKT/mTOR pathway alterations
	ER signaling	ER-PgR expression
T-DM1	Impaired HER2 binding	p95HER2; MUC4 expression
	Parallel/downstream signaling	NRG, HER2-HER3, *PIK3CA* mutations
	T-DM1 internalization/release	SLC46A3, MDR1
Trastuzumab plus Lapatinib (T + L)	Impaired HER2 binding	Low HER2 levels
	FGFR1 signaling	*HER2* mutations
	Downstream pathways	*FGFR1* amplification
	ER signaling	*PI3KCA* mutations,
	Cell cycle regulation	ER-PgR expression
		Cyclin D1-CDK 4/6 expression
Trastuzumab plus Pertuzumab (T + P)	Altered intracellular pathways	*PIK3CA* mutations
	HER2 signaling	*HER2* mutations

In breast cancer…

As far as potential mechanisms of resistance to T-DXd, driver alterations were identified in at least 3% of samples and those founded in baseline samples were associated with upfront resistance. However, 6% (5/88) of patients presented an *ERBB2* hemizygous deletion at baseline and four of them did not respond to T-DXd.

IHC for HER2 was assessed both in baseline and PD samples, and a decrease of HER2 expression at PD, as secondary resistance mechanism, was found in 65% (13/20) of patients.

Genomic alterations were assessed by WES in 20 PD samples, half of whom were matched with baseline biopsies. Interestingly, mutations of *SLX4* gene, encoding a DNA-repair protein which regulate the endonucleases, were detected in 20% (4/20) of PD biopsies; half of them were acquired and the other 2 missed the matched baseline samples to perform the WES [44].

According to this evidence, BC cell lines depleted for *SLX4* were treated with DXd for 5 days and, interestingly, a higher quantity of DXd was required to kill them. Therefore, *SLX4* loss of function mutations could mediate resistance to the anti-topoisomerase 1 (TOP1) activity of the payload (deruxtecan) [43].

In conclusion, the decrease of HER2 expression and *SLX4* loss of function mutations represent the first evidences of mechanisms of resistance to T-DXd.

In lung cancer…

J Thorac Oncol. 2023 Jul 8;S1556-0864(23)00666-4. doi: 10.1016/j.jtho.2023.06.020. Online ahead of print.

MET Fusions in NSCLC: Clinicopathologic Features and Response to MET Inhibition

Richard Riedel [1], Jana Fassunke [2], Andreas H Scheel [2], Matthias Scheffler [1], Carina Heydt [2], Lucia Nogova [1], Sebastian Michels [1], Rieke N Fischer [1], Anna Eisert [1], Heather Scharpenseel [1], Felix John [1], Lea Ruge [1], Diana Schaufler [1], Janna Siemanowski [2], Michaela A Ihle [2], Svenja Wagener-Ryczek [2], Roberto Pappesch [2], Jan Rehker [2], Anne Bunck [3], Carsten Kobe [4], Felix Keil [5], Sabine Merkelbach-Bruse [2], Reinhard Büttner [2], Jürgen Wolf [6]

Affiliations + expand

PMID: 37429463 DOI: 10.1016/j.jtho.2023.06.020

Abstract

Introduction: MET fusions have been described only rarely in NSCLC. Thus, data on patient characteristics and treatment response are limited. We here report histopathologic data, patient demographics, and treatment outcome including response to MET tyrosine kinase inhibitor (TKI) therapy in MET fusion-positive NSCLC.

Methods: Patients with NSCLC and MET fusions were identified mostly by RNA sequencing within the routine molecular screening program of the national Network Genomic Medicine, Germany.

Results: We describe a cohort of nine patients harboring MET fusions. Among these nine patients, two patients had been reported earlier. The overall frequency was 0.29% (95% confidence interval: 0.15-0.55). The tumors were exclusively adenocarcinoma. The cohort was heterogeneous in terms of age, sex, or smoking status. We saw five different fusion partner genes (KIF5B, TRIM4, ST7, PRKAR2B, and CAPZA2) and several different breakpoints. Four patients were treated with a MET TKI leading to two partial responses, one stable disease, and one progressive disease. One patient had a BRAF V600E mutation as acquired resistance mechanism.

EXPERT OPINION POST MDT

- MET non-canonical fusion potentially actionable
- For Orthogonal Testing – MET Immunohistochemistry in Amsterdam, possible fusion testing using ARCHER
- IF MET over expressed by IHC consider Crizotinib
- eGFR = 33 ml/min – could use Crizo with dose modification

What has been our MTB journey?

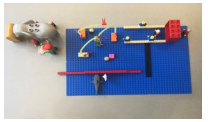
2019

Meeting with government stakeholders

Met NCCP, HRB, HIQA, Novartis and a patient organization to transparently communicate the programme objectives and get their input

Ideation session

Initial MTB program co-designed with Roche, Irish clinicians, and local patient organisation (SJK)



2020

Co-creation of an MTB Pilot

Collected insights and needs from selected HCPs to jointly design the MTB Pilot in Ireland

First MTB Session

1st MTB pilot session in November with 2 patient cases and 5 participants

2021

Extension of the MTB pilot

MTB pilot extended as the number of patient cases, participants and program appreciation increased

Collaboration agreement signed with CTI

Cancer Trials Ireland onboarded for handover of operations for program

2022

Cancer Trials Ireland MTB

July: Full operating of MTB program by CTI, no more involvement of Roche in operations or access to MTB information

2023

Evolution of CTI MTB

Introduction of Haem/Onc MTBs, Educational webinars, Research studies in development

Next steps

Participation in European MTB network to develop consensus standards and patient outcome registry

To date: 66 solid tumour and 5 haem/onc **cases discussed**

Next Steps in Ireland for Molecular MTB – in discussion with NCCP (Irish government)

Screen Requests for Public Access to Cancer NGS

Allow off label prescribing of targeted therapies

Link to Clinical Trials

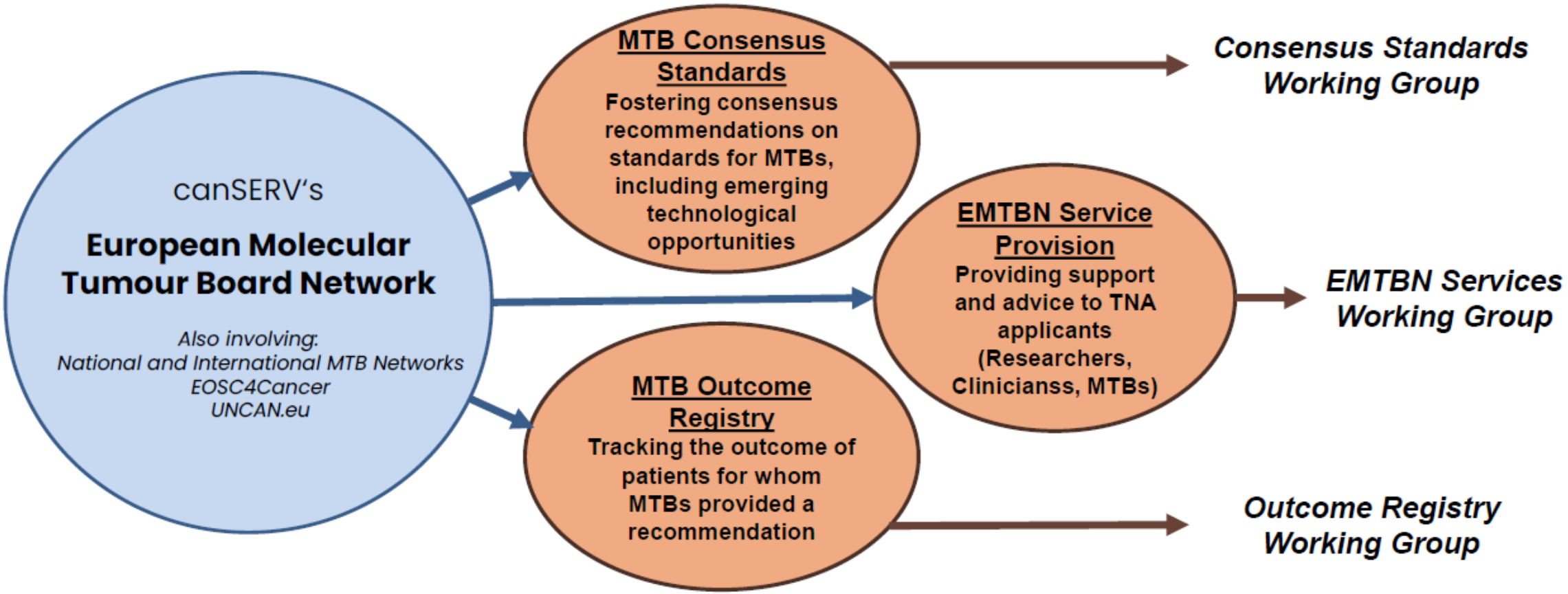
Prioritize referral to Hereditary Cancer Genetics

Suggestions for National or Regional MTB

- Have a template for presenting team to fill in
- Decide on inclusion and exclusion criteria – Italy has a Gynae only MTB!
- Decide if cases need to be anonymized for legal (GDPR) and liability reasons
- Initially clinicians may ask questions that experts see as trivial but as expertise builds quality of discussion improves exponentially
- Provide a printed MTB report to clinician (and CME points)
- Get patient consent to gather data prospectively – get published!
- Consider a limited number of free or discounted tests to establish experience using NGS
- Join European MTB Network

European Molecular Tumour Board Network: objectives

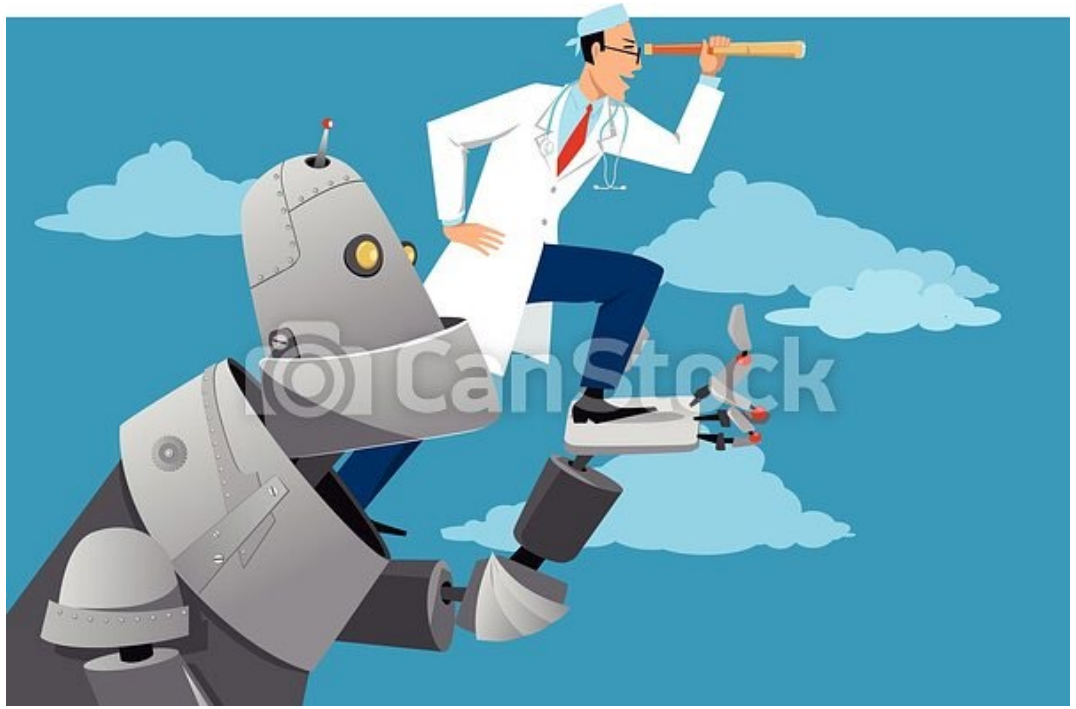
canSERV
providing cutting edge cancer research services across europe



Funded by the European Union
Grant agreement No. 101058620

www.canserv.eu/expert-network

The Future?



- Geneticist and Data Scientist at every MDT meeting in every hospital
- Sequence the genome of patient, cancer, microbiome etc.
- Artificial Intelligence suggests clinical trials and targeted therapies
- Drugs printed in hospital pharmacy

Molecular Tumour Boards as a bridge to the Future

- Enable busy clinician who treats multiple tumour types to use NGS safely
- Helps trainees get exposure to world experts
- Triggers interest in on line Clinical Genetics course provided by RCPI
- Patients may not get a new drug or survival benefit BUT they know no stone was left unturned in seeking best possible care

Bon Secours Cork Cancer Centre

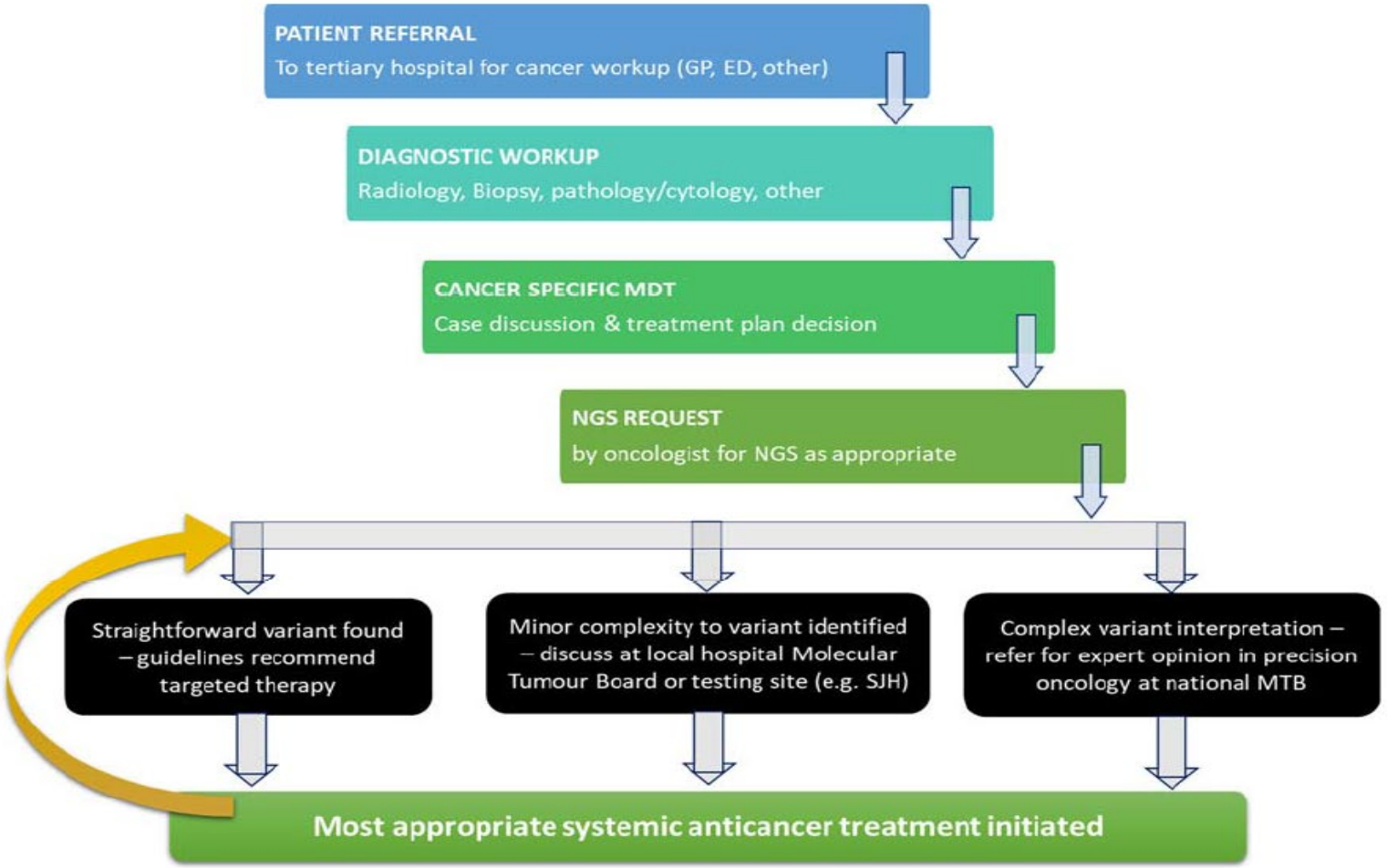
Thank you for listening

And thank you to my daughter; Suzanne, who is awesome and who made these slides look tolerable ☺ who I love more than my dog.

Any Questions?

Submission to the MTB

DECISION TREE



Abstract e13533:
Developing the educational Molecular Tumour Board in Ireland: pilot to national initiative

Authors: Dearbhaile Collins[1], Deirdre Poretti[2], Verena Murphy[1], Mathias Ganter[3], Romina Girotti[3], Ray McDermott[4], Brian Healey Bird[5], Marie Dominique Galibert[6], Rodrigo Dienstmann[7], Terri McVeigh[8], Stephen Finn[9]

Affiliations: [1] Cancer Trials Ireland, [2] Roche Ireland, [3] Accenture, Basel, Switzerland, [4]Tallagh University Hospital, Dublin, Ireland 5, Bon Secours Hospital, Cork Ireland, 6

BACKGROUND

The era of genomics, powered by next generation sequencing (NGS), has revealed the potential to associate genomic alterations with targeted treatments to treat cancer patients. A major challenge for oncologists is to interpret and action the findings of multi-gene sequencing.

Molecular Tumour Boards (MTBs) already exist in leading international medical centres and oncologists and care teams attend them regularly to discuss relevant patient cases. An MTB is an interdisciplinary meeting where cancer patients with previous molecular profiling by NGS are discussed. MTBs bring together various professionals who help oncologists to interpret molecular profiles.

Oncologists in Ireland have limited access to targeted therapies and there is a very limited number of clinical cancer trials. Molecular profiling by NGS is not very well established and oncologists have limited knowledge of the interpretation of NGS data.

To tackle this, Roche Ireland wanted to support the establishment of an educational MTB. The aim was to improve cancer patients´ care by providing the treatment team with insights through a multidisciplinary discussion on the genomic findings, their clinical implications, and potential treatment options.

METHODS

The MTB in Ireland was established in November 2020 as a cross-institutional, educational and multi-disciplinary pilot and expanded nationally under Cancer Trials Ireland as a resource for clinicians and other oncology groups.

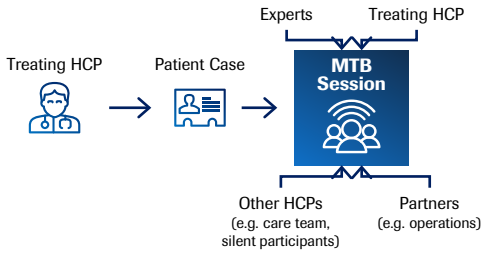
The guiding principles for the creation of the MTB in Ireland are:

01	02	03	04	05
Nimble (pilot, learn, optimize)	Selected medical centres in Ireland	Foster collaboration among medical centres	Long term self-sustaining ecosystem	Roche is not participating in any MTB session

CO-CREATION – CO-BENEFITTING – CO-EDUCATION

The guiding principles for patient inclusion are:

i) Metastatic solid organ cancers, ii) Somatic mutations (no germline mutations during pilot phase), iii) Urgency of the treatment for the patient, iv) Multiple identified targets / complex genomics, v) Interesting genomics considering the clinical history and vi) Novel alterations.



During a virtual MTB session, health care professionals (HCPs) from selected hospitals will be able to:

- Discuss **their clinical cases** (no anecdotal/educational cases)
- Get **insights from highly experienced experts** in molecular profiling
- Get **insights** from other HCPs (beyond their local network)
- Improve their **awareness** of cancer genomics and diagnostic testing, personalized cancer care, and genomic research

CONCLUSIONS

Between November 2020 and December 2021, the educational Molecular Tumor Board in Ireland transitioned from a pilot to a National initiative where 30 patient cases were discussed, and 157 participants took part of the sessions. Additionally, 16 institutions participated in the discussions as silent or active participants. If treatment impact is a measure of success, then it's worth noting that 80% of the oncologists involved said that they have either confirmed or changed their patient treatment plans based on the insights shared during the meeting. In December 2021, Roche Ireland and Cancer Trials Ireland (CTI), a leading independent cancer research organization, agreed to continue offering the MTB and evolve the initiative by, for example, collecting data related to clinical outcomes and genomic findings based on the patients discussed during the MTB sessions.

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RESULTS

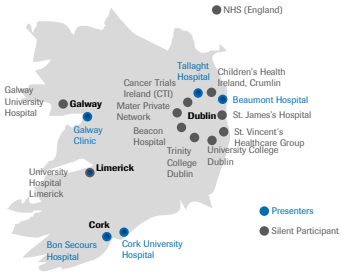
Setup of an individual MTB session

All Metastatic patients	**All** Panels	**1 T&C** Anonymized, insights
1h Duration (on average)	**≥ 1** Hospital (per session)	**1** Patient case template
2w Submission window	**4 weeks** Recurrence	**4** Patient cases (up to)

Within an MTB session, up to four patient cases from all metastatic and localized adult cancer patients are discussed. There is a two-week window for patient case submission. The duration of the MTB session is usually one hour, during which up to four treating physicians present four patient cases (one each) from one or more hospitals. The MTB is held with the scientific contribution of three international experts: Dr Rodrigo Dienstmann, Dr Marie Dominique Galibert, and Dr Terri McVeigh, and local expert Dr Stephen Finn.

Medical centers and organizations involved

The first MTB in Ireland was conducted in November 2020 with five participants and two patient cases. Between November 2020 and December 2021, the program grew to a monthly meeting where a total of 30 patient cases have been discussed and 157 participants have been part of the Irish MTB (including 16 institutions as silent or active participants). There are typically four patient cases and nearly twenty participants per session.



Key findings

100% Participants admitted that **MTBs** they attended met, exceeded or significantly exceeded their **expectations**

90% Presenters confirmed that **experts communicated effectively**

87% Participants considered the discussions on **clinical implications of targeted therapies or immunotherapies** associated with genomic alterations as the **most valuable component**

80% Presenters confirmed that the MTB discussions helped to **confirm, modify or change the treatment plan** for at least one of their patients

65% Participants were **very satisfied with the insights** shared around molecular profiling and biological pathways

24% **Silent participants** would like to **submit a patient case** in one of the upcoming MTB session (3 oncologists & 2 molecular biologists)

FUTURE DIRECTIONS FOR RESEARCH

The Ireland MTB Ireland will maintain the educational service and develop a cancer database / registry for the collection of discussion points from the patient discussions and outcomes.