La révolution numérique a atteint l'Oncologie

PROJET WATSON

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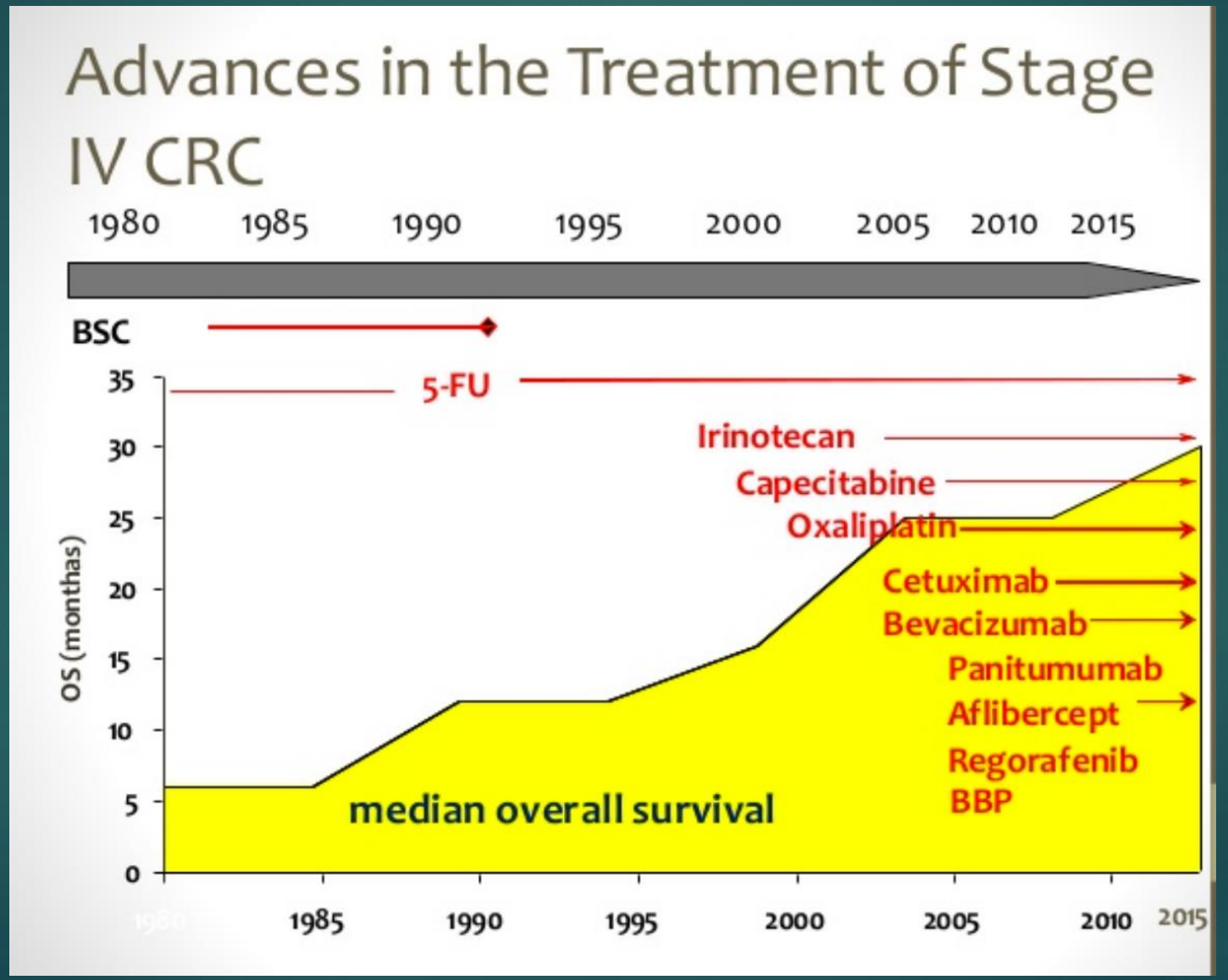
Président, Institut National du Cancer

L'oncologie: evolution en 30 ans… en 10 dias ☺

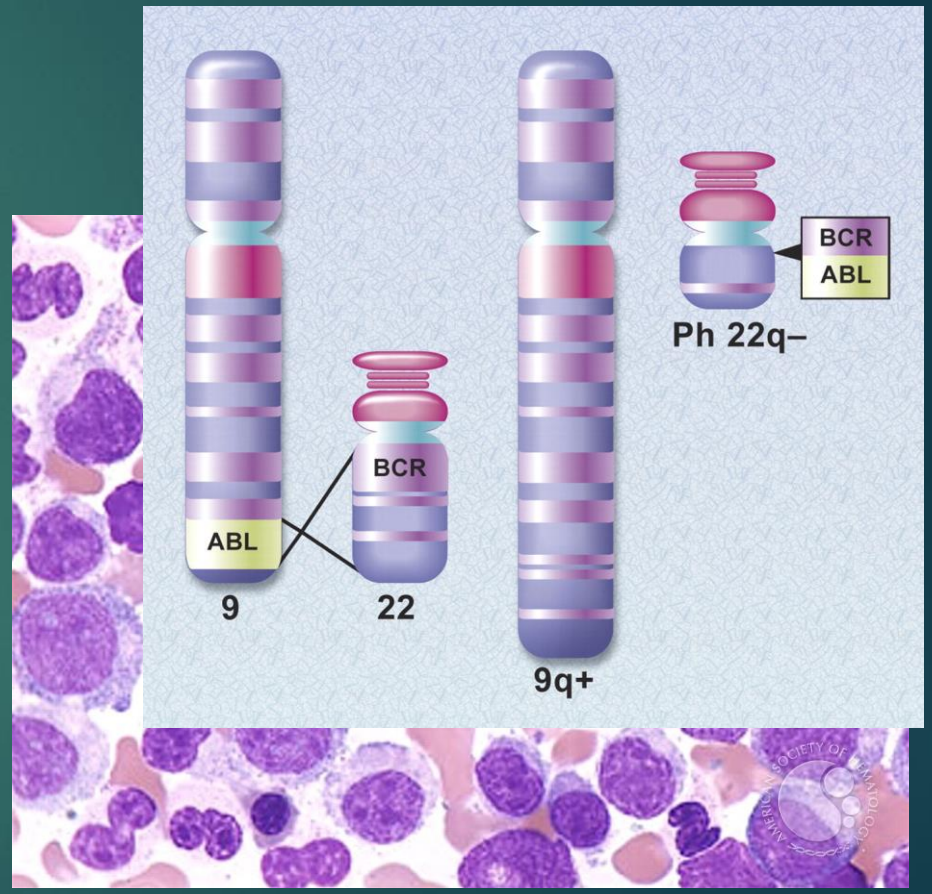
- du concept de "mouroir" à une possibilité de "guérison" dans un nombre significatif de cas….
- Leucémie chez l'enfant
- Tumeurs du testicule
- Lymphomes de Hodgkin
- Leucémie myéloïde chronique
- Autres: Sein, colon…

Le cancer du colon métastatique

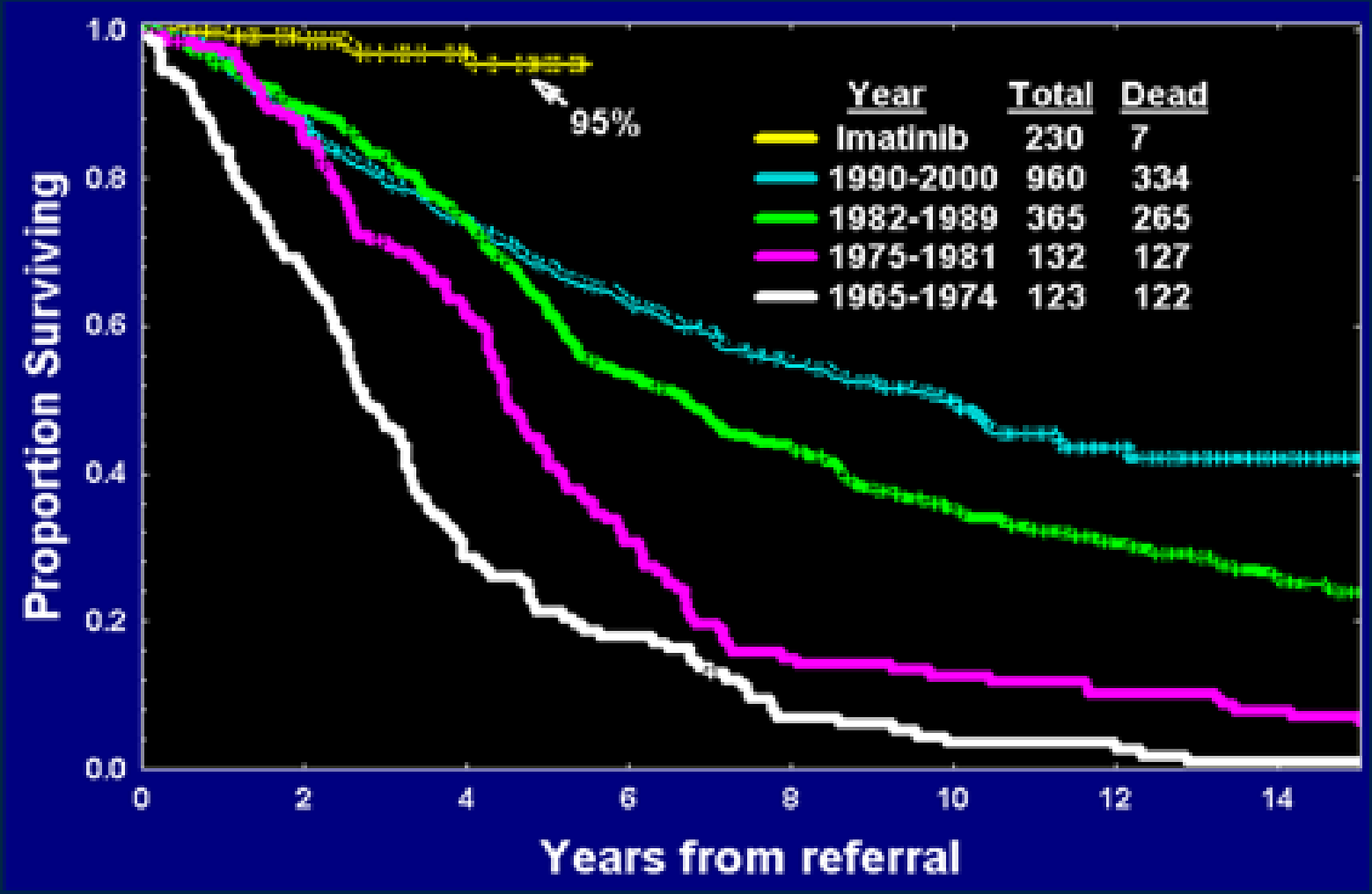


Médicaments ciblés
Leucémie Myéloïde chronique

- La cible => altération moléculaire spécifique (translocation chromosomique 9;22 (BCR-ABL))
- Oncogène puissant faisant se multiplier les cellules de la moëlle



Survival in Early Chronic Phase CML

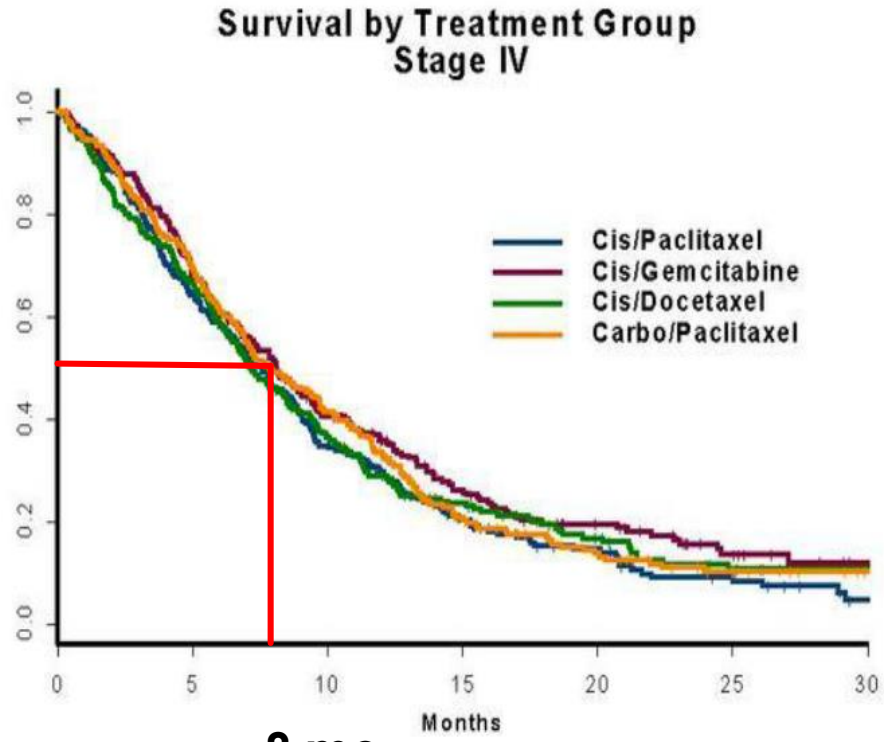


Quintás-Cardama A, Cortes JE. *Mayo Clin Proc*. 2006;81:973-988.

Cancer du Poumon

Platinum-Based Doublets for NSCLC

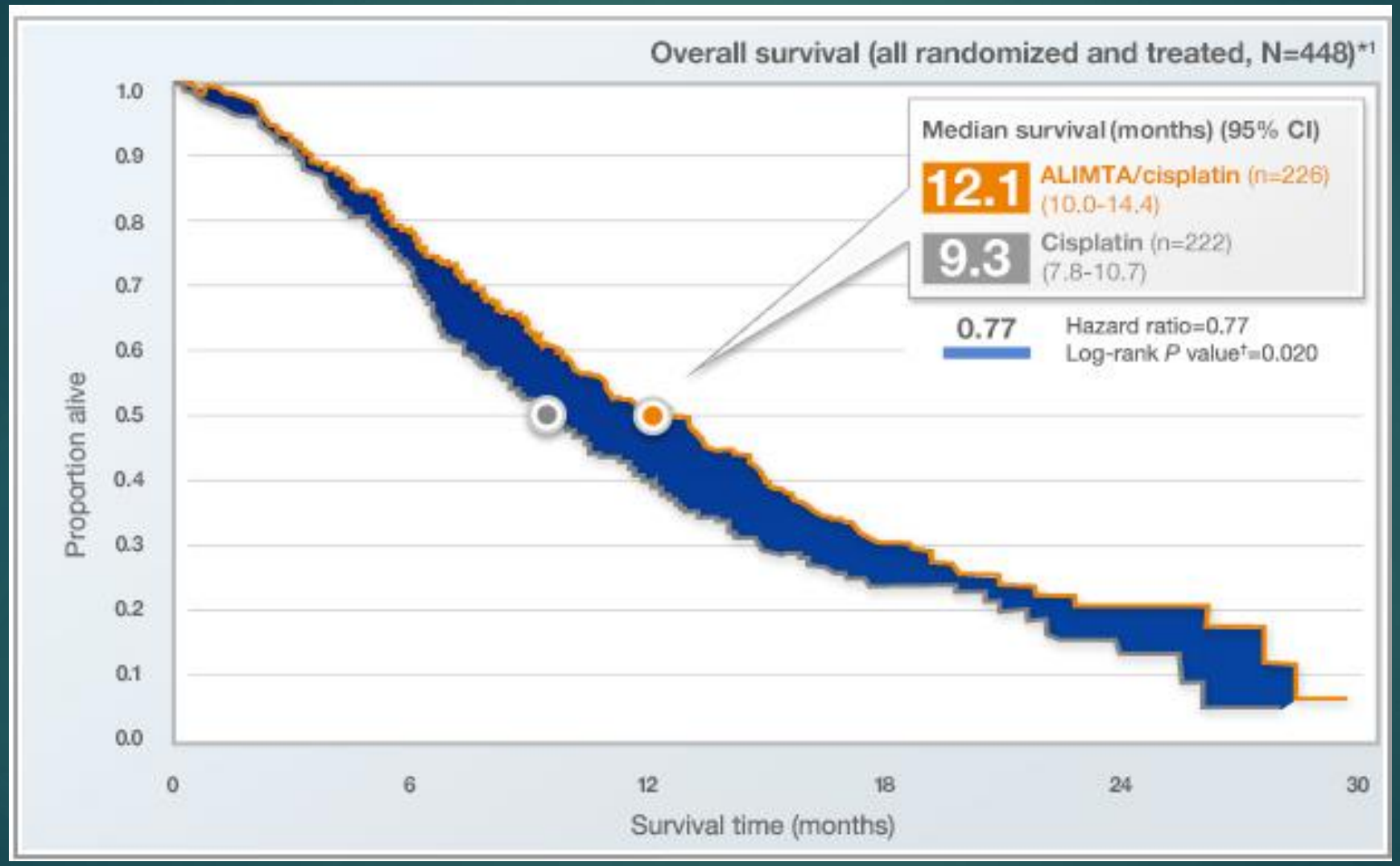
North American Experience (ECOG)



8 mo

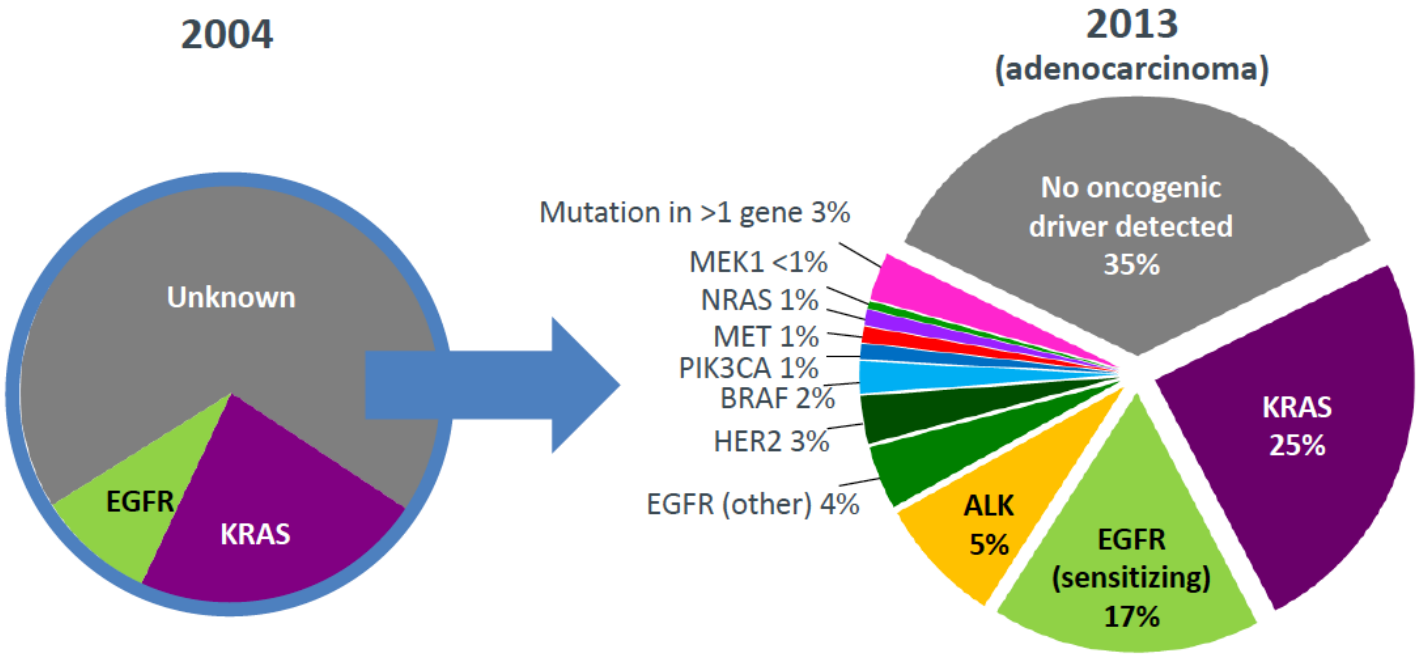
Schiller JH, et. al. *N Engl J Med.* 2002;346(2):92-98.

Meilleure chimiothérapie



Meilleurs biomarqueurs

Evolving Molecular Classification of NSCLC Over the Last Decade

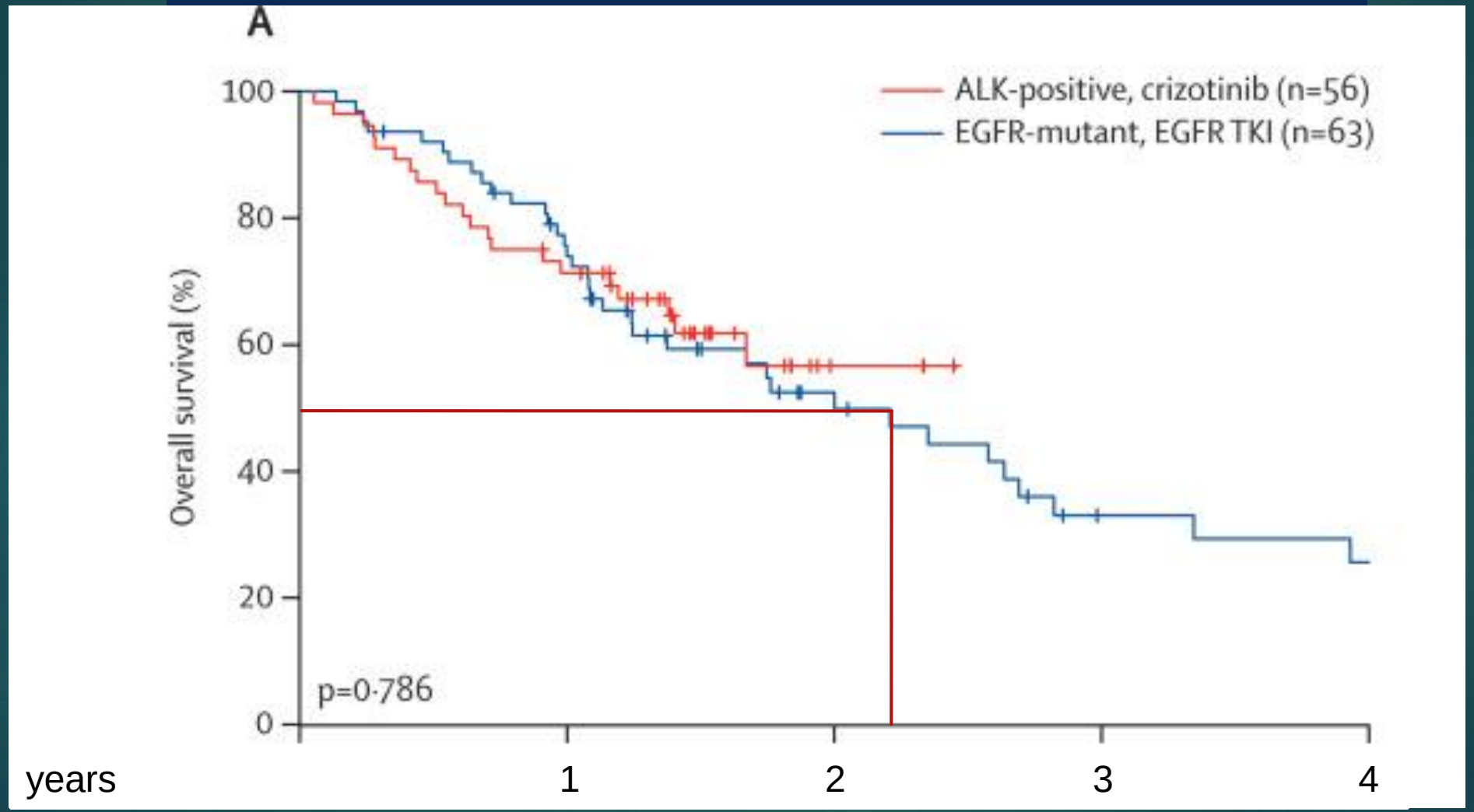


- Clinical practice has moved into an era of precision medicine in which many cancer patients are treated with targeted therapies (TKIs)

Pao & Girard. Lancet Oncol 2011; Blakely & Bivona. Cancer Discov. 2012; Johnson, et al. ASCO 2013

ALK

ORR: 93.5% (95%CI: 82.1 - 98.6)



Comment faire avancer cette révolution encore plus vite?

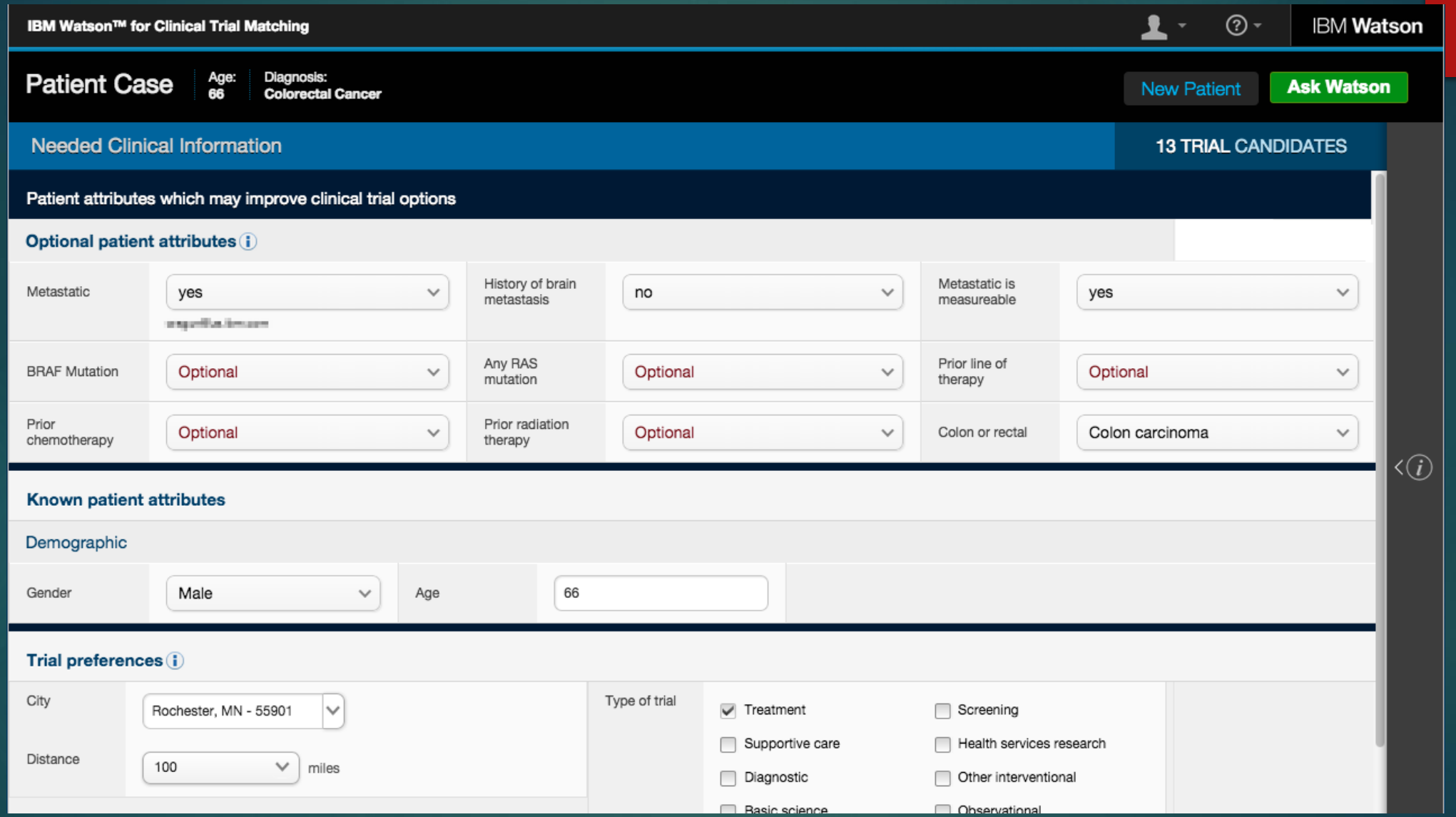
L'intelligence artificielle

IBM-Watson


PIENSE
THINK
ΣΚΕΨΟΥ
DENKE
PENSER
$300,000
$1,000,000
$200,000
KEN
WATSON
BRAD

Que sait faire Watson?

- Watson est une intelligence artificielle développée par IBM (Deep Blue)
- Sait lire et comprendre du texte libre….
- Connaît toute la littérature médicale…
- Il est programmé pour proposer des décisions médicales.
- Il peut être paramétré pour respecter des « guidelines » nationales
- Existe pour cancer du sein, colon, poumon, bientôt sarcomes
- Module Médecine personnalisée moléculaire


IBM Watson™ for Clinical Trial Matching
IBM Watson
Patient Case
Age: 66
Diagnosis: Colorectal Cancer
New Patient
Ask Watson
Needed Clinical Information
13 TRIAL CANDIDATES
Patient attributes which may improve clinical trial options
Optional patient attributes
Metastatic
yes
History of brain metastasis
no
Metastatic is measureable
yes
BRAF Mutation
Optional
Any RAS mutation
Optional
Prior line of therapy
Optional
Prior chemotherapy
Optional
Prior radiation therapy
Optional
Colon or rectal
Colon carcinoma
Known patient attributes
Demographic
Gender
Male
Age
66
Trial preferences
City
Rochester, MN - 55901
Distance
100
miles
Type of trial
Treatment
Screening
Supportive care
Health services research
Diagnostic
Other interventional
Basic science
Observational


IBM Watson for Oncology
Treatments
CMF (Cyclophosphamide/ Methotrexate/ Fluorouracil)
TC (Docetaxel/ Cyclophosphamide)
CEF (Cyclophosphamide/ Epirubicin/Fluorouracil)
CAF (Cyclophosphamide/ Doxorubicin/
Details for CMF
Rationale
Additional Publications
Administration
Rationale supporting this treatment
This is recommended when the patient has a high Oncotype DX
MSK curated literature about this treatment
Two months of doxorubicin-cyclophosphamide with
reinduction therapy compared with 6 months of cyc
methotrexate, and fluorouracil in positive-node brea
tamoxifen-nonresponsive tumors: results from the N
Breast and Bowel Project B-15.

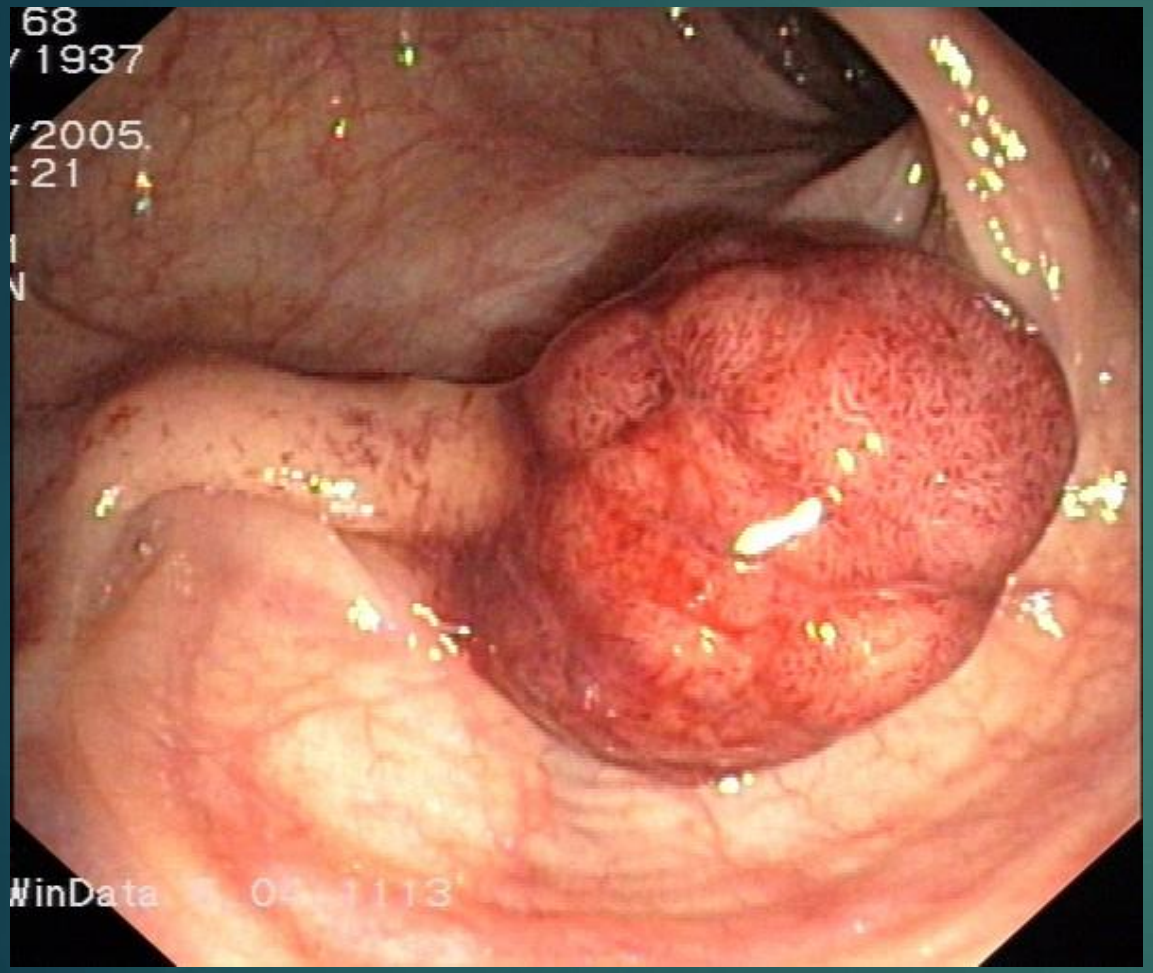
QUE PEUT L'ANALYSE MOLÉCULAIRE DE LA TUMEUR NOUS APPRENDRE…?

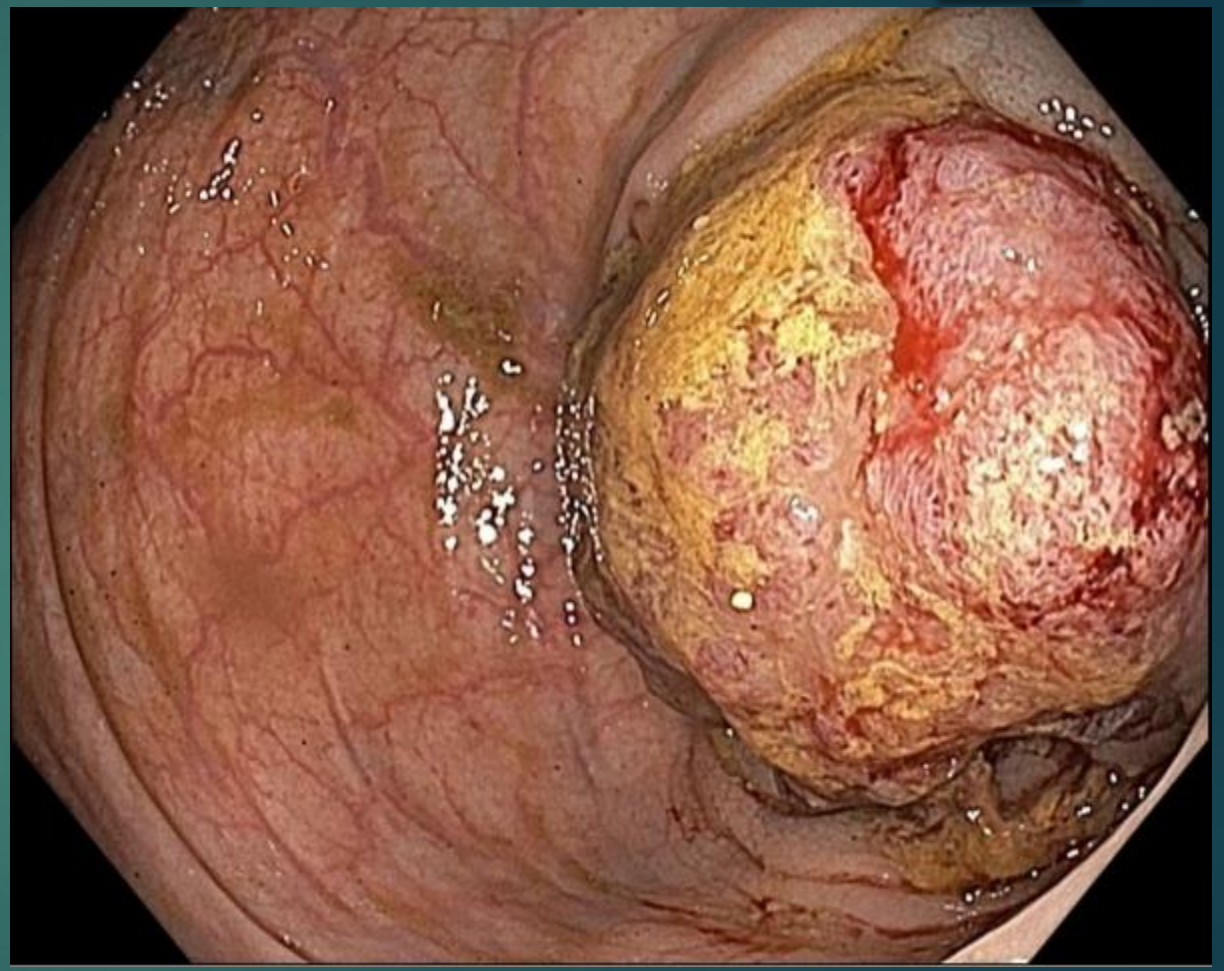
Le Profilage moléculaire

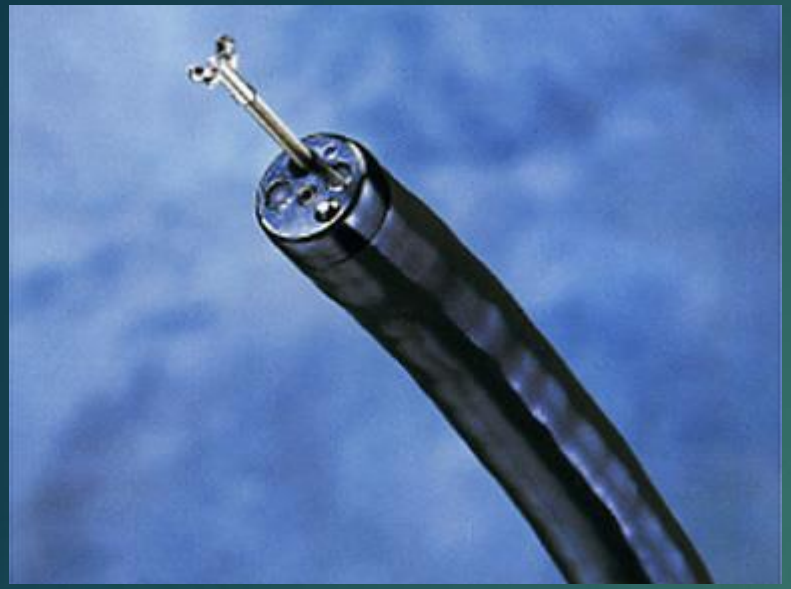
IBM WATSON GENOMIC ANALYTICS AT SANFORD CANCER CENTER

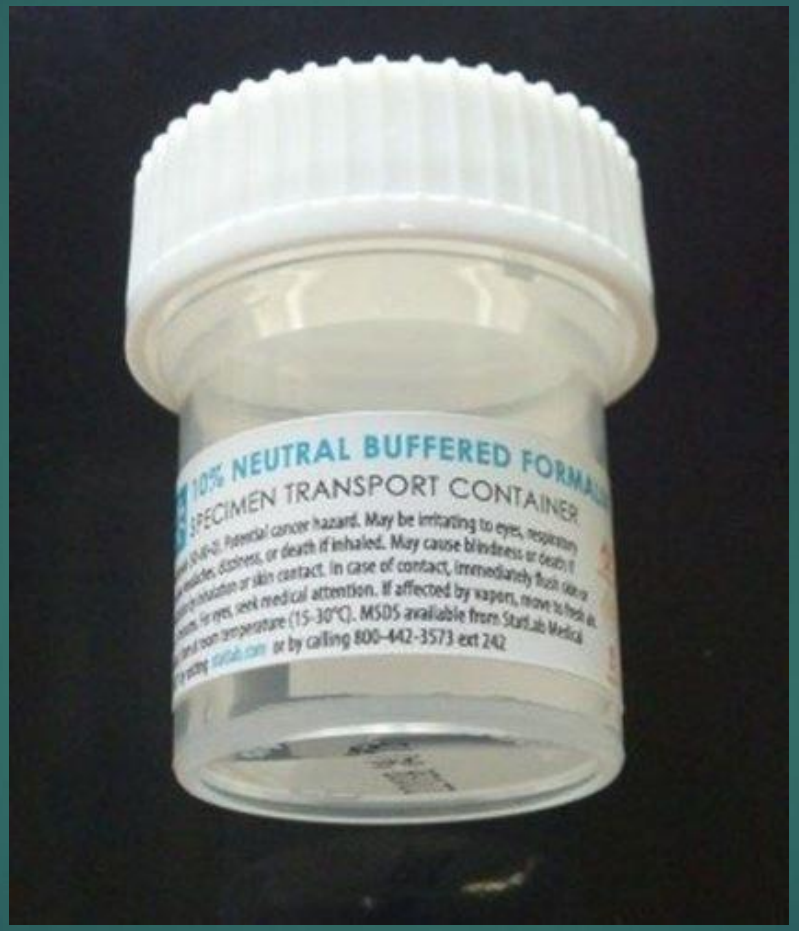
A New Era in Personalized Cancer Treatment

What took weeks, now takes minutes. IBM Watson Genomic Analytics is able to sort through and analyze the DNA data of cancer patients and quickly provide comprehensive insights on cancer-causing mutations faster than ever before. The

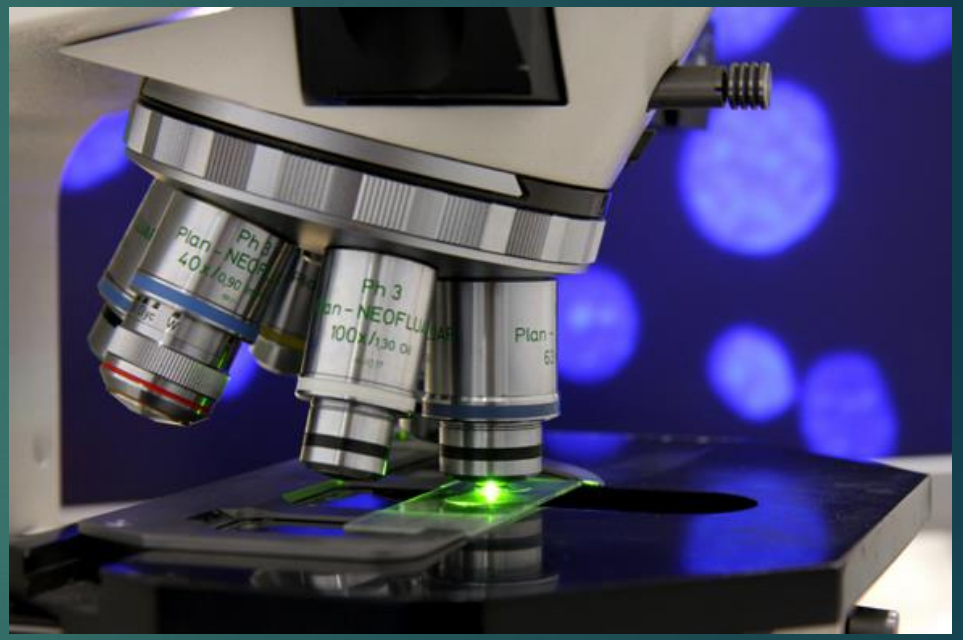

68
1937
2005
21
WinData

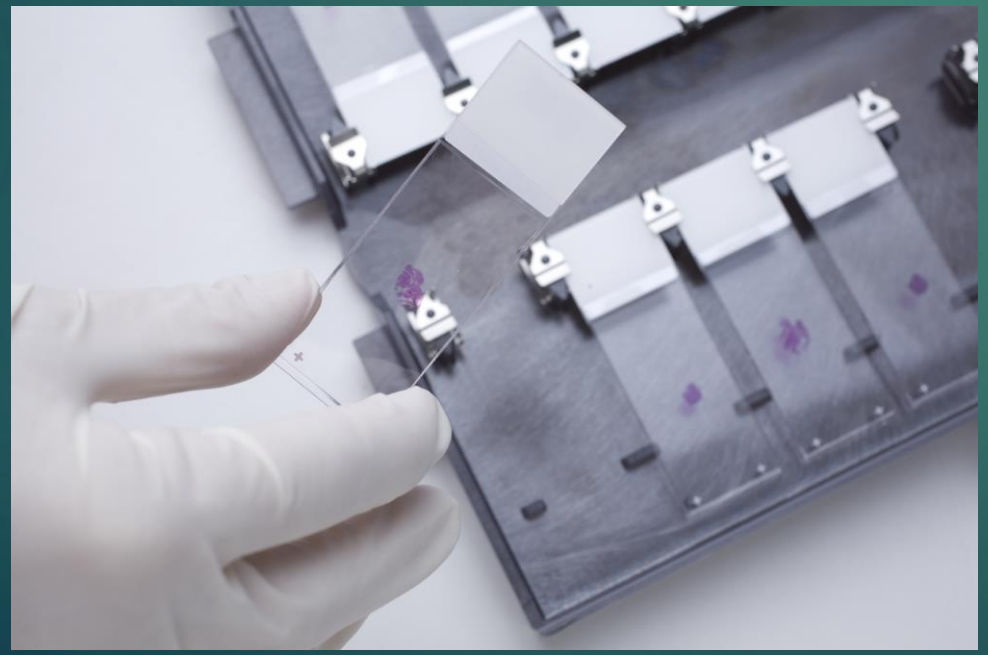


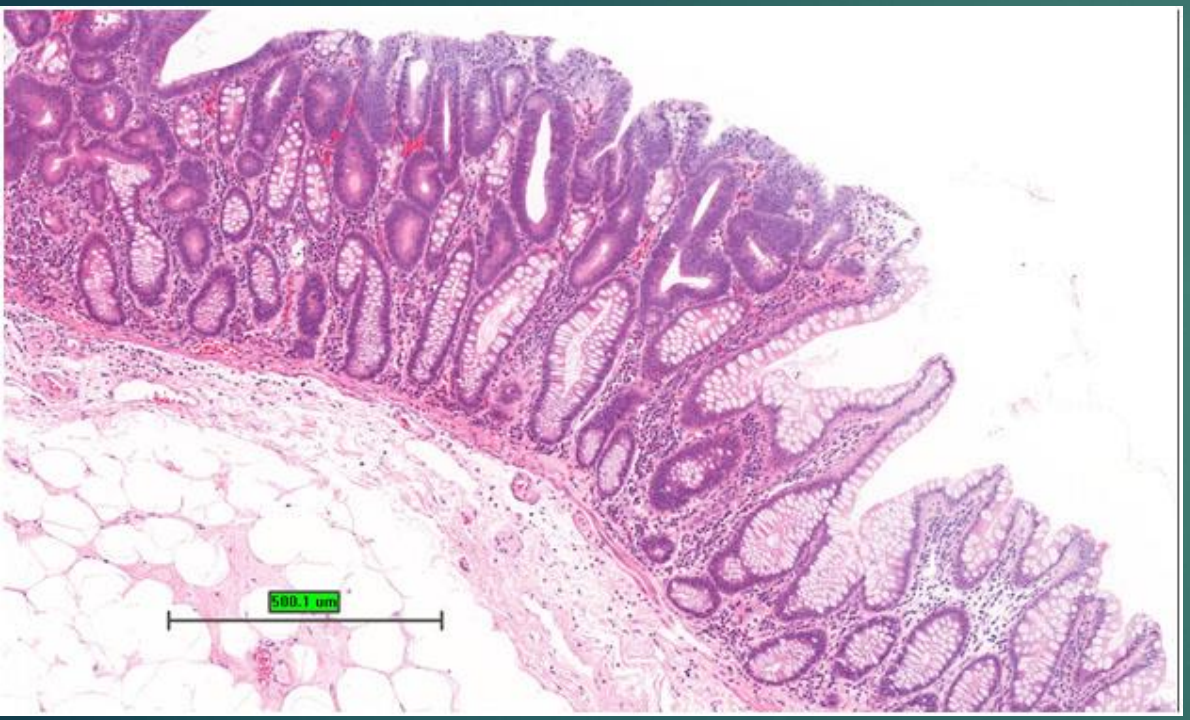


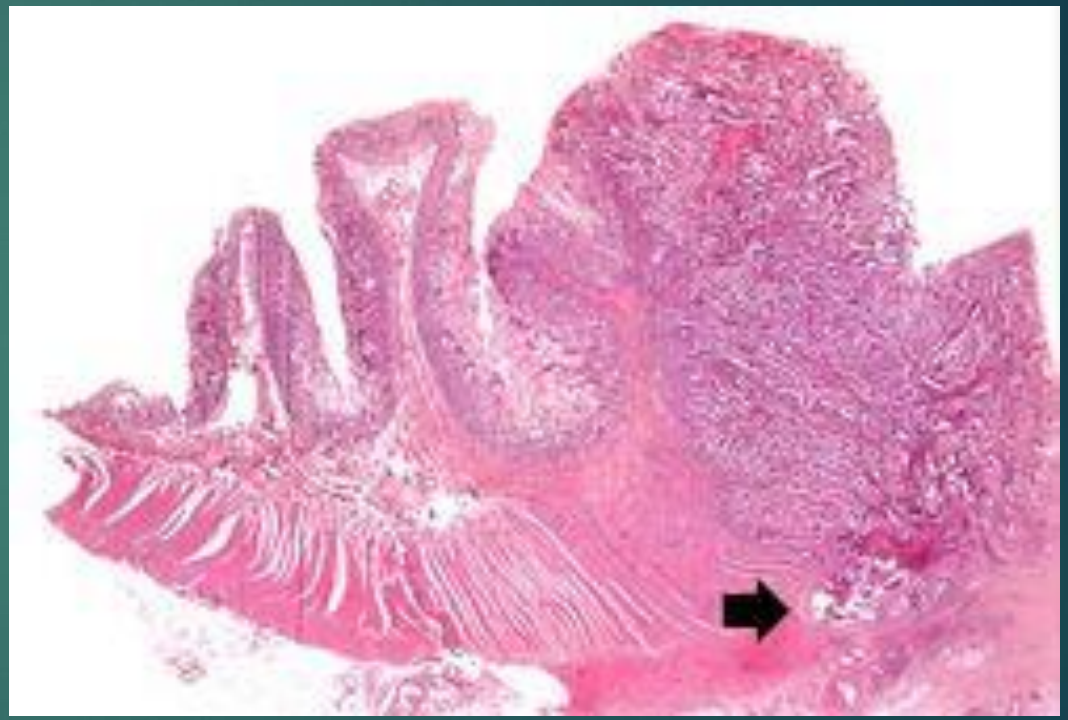

10% NEUTRAL BUFFERED FORMA
SPECIMEN TRANSPORT CONTAINER

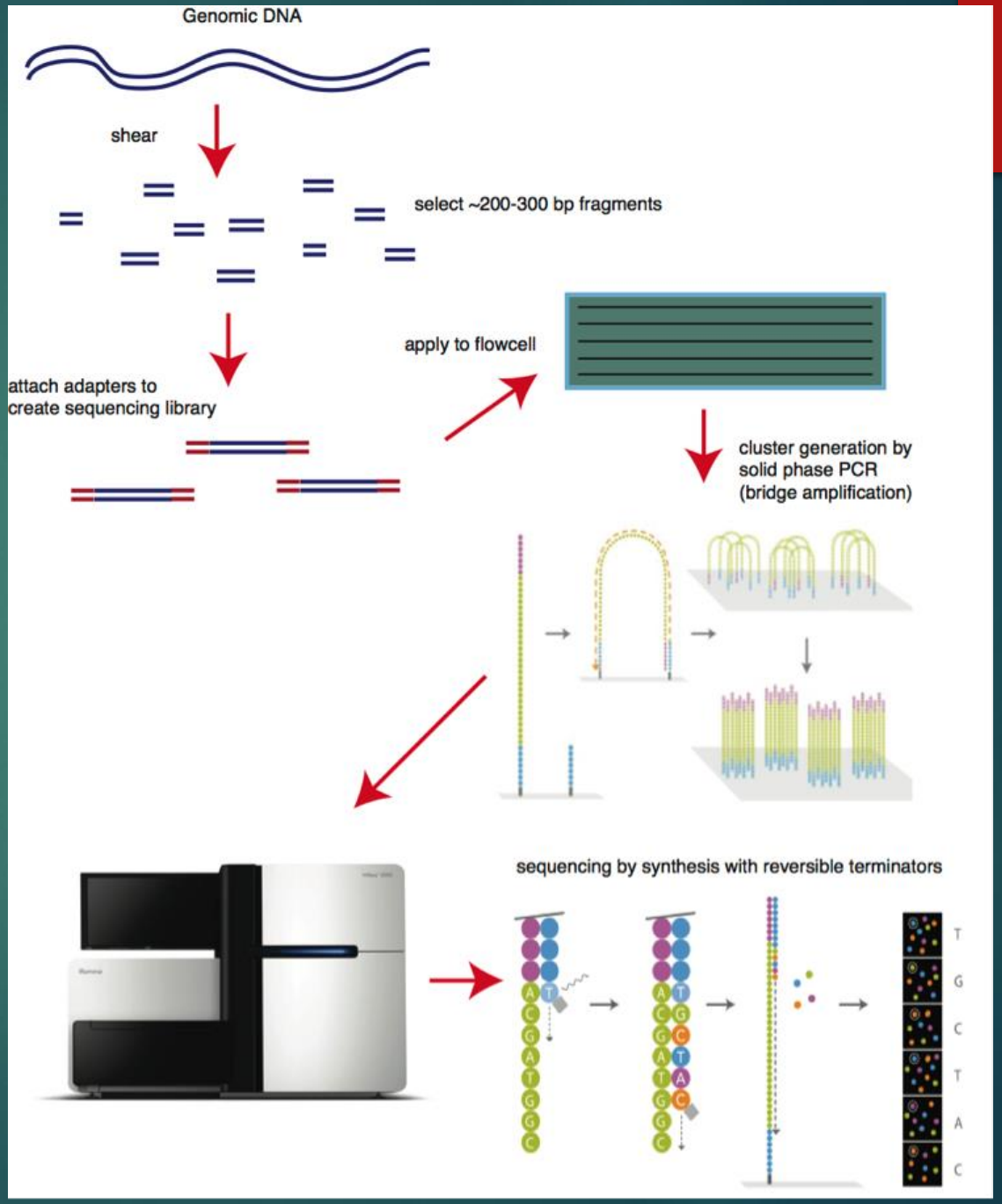

Leica
MEDICAL EQUIPMENT SOURCE, LLC

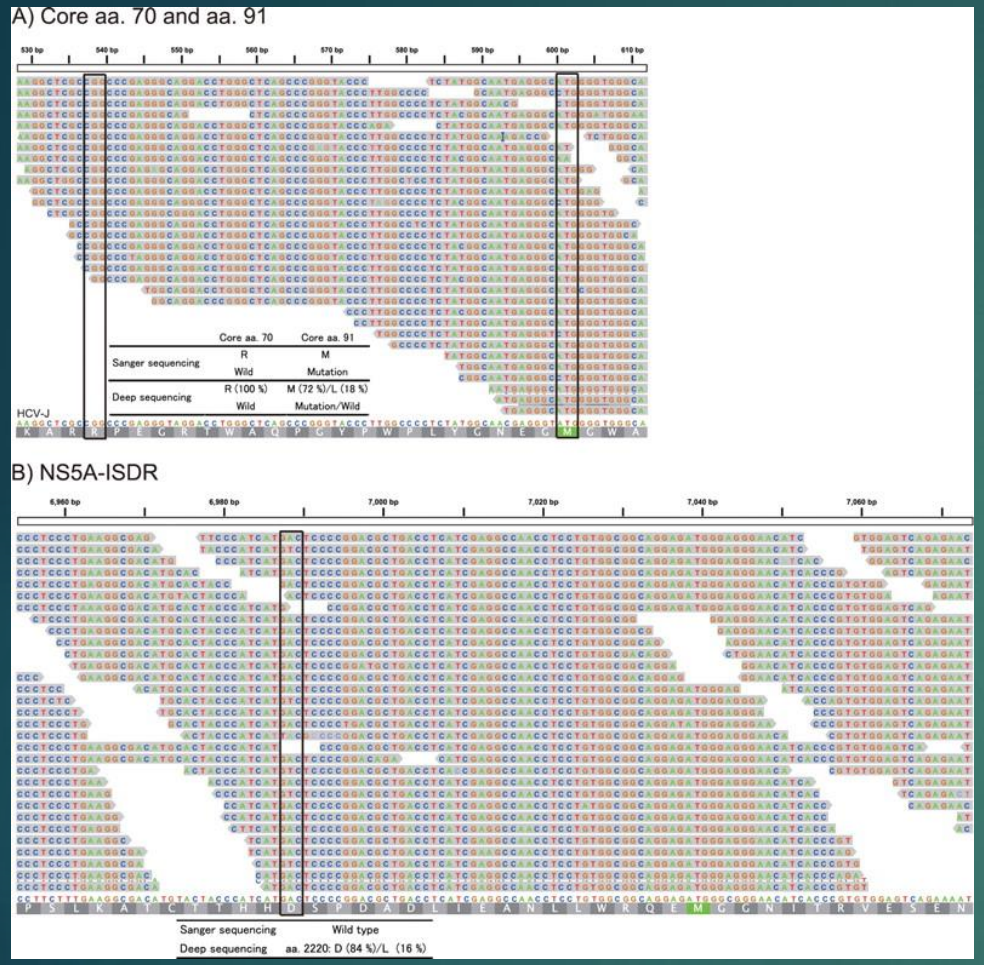

Ph 3
100x/1,30 Oil

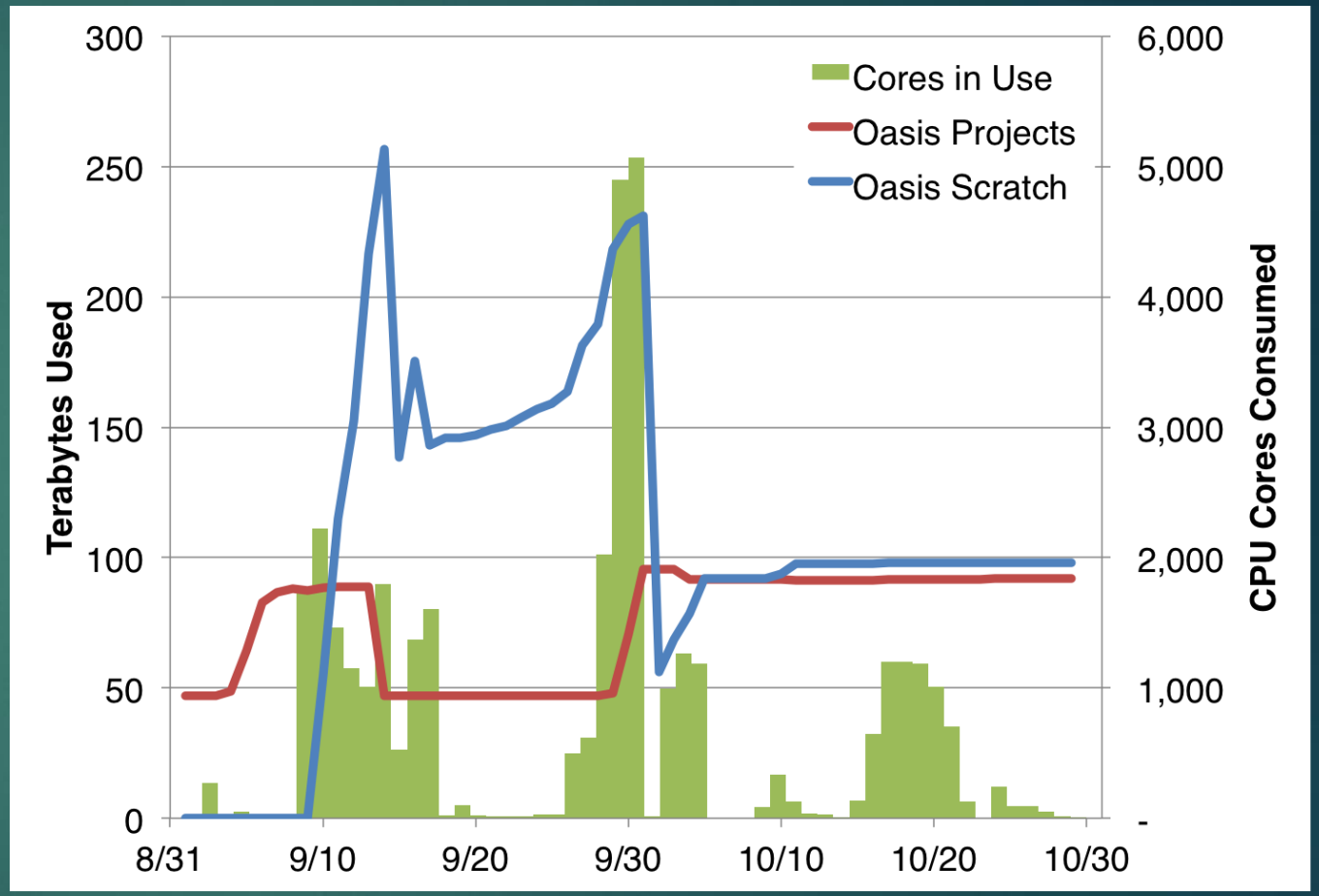



500.1 um




Genomic DNA
shear
select ~200-300 bp fragments
apply to flowcell
attach adapters to
create sequencing library
cluster generation by
solid phase PCR
(bridge amplification)
sequencing by synthesis with reversible terminators
T
G
C
T
A
C





=> Des « tonnes » de données

Molecular testing:

List of genes for mutations

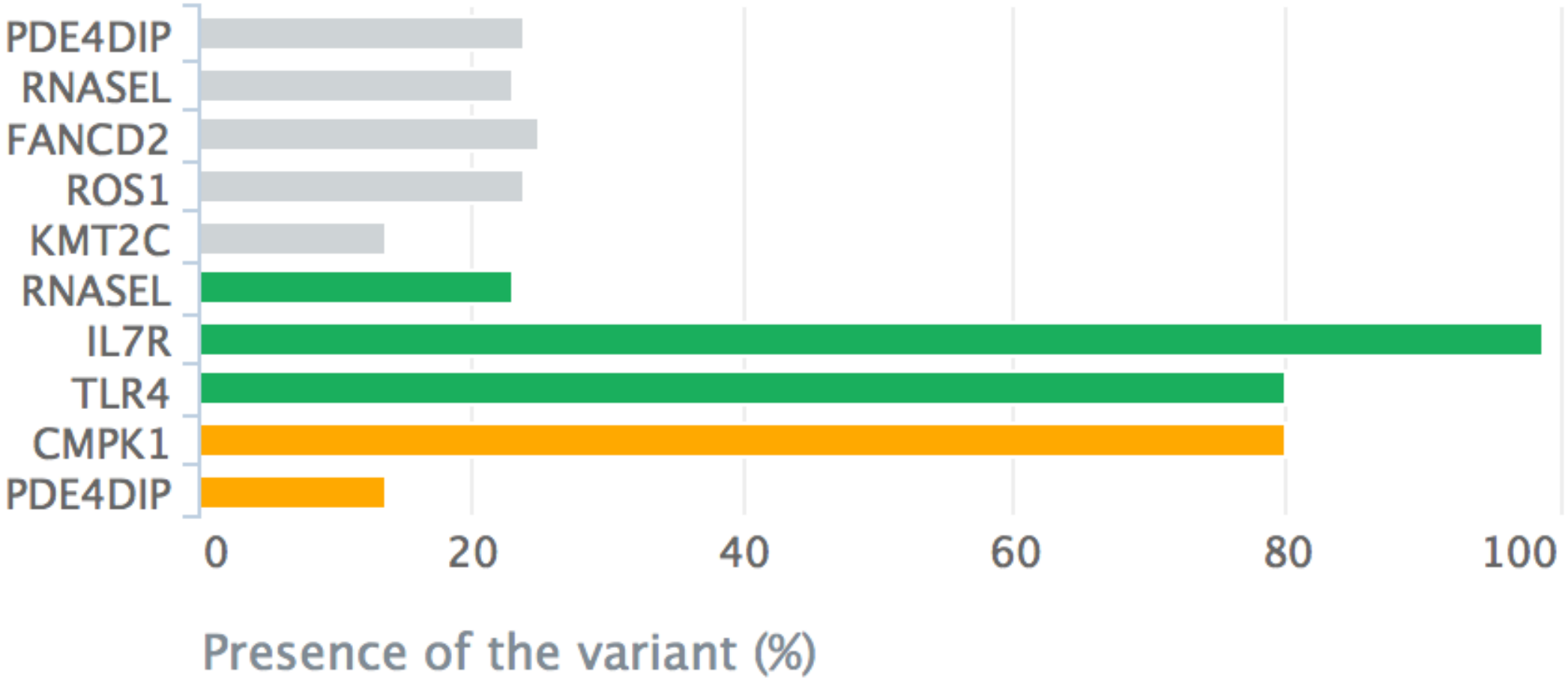
● Damaging variants ● Potentially damaging ● Unknown

ABL1	ABL2	ACVR2A	ADAMTS20	AFF1	AFF3	AKAP9	AKT1	AKT2	AKT3
ALK	AMER1	APC	AR	ARID1A					
ATR	ATRX	AURKA	AURKB	AURKC					
BCL11B	BCL2	BCL2L1	BCL2L2	BCL3					
BIRC5	BLM	BLNK	BMPR1A	BRAF					
CASC5	CBL	CCND1	CCND2	CCNE1					
CDH2	CDH20	CDH5	CDK12	CDK4					
CEBPA	CHEK1	CHEK2	CIC	CKS1B					
CRKL	CRTC1	CSF1R	CSMD3	CTNNA1					
DCC	DDB2	DDIT3	DDR2	DEK					
EML4	EP300	EP400	EPHA3	EPHA7					
ERBB4	ERCC1	ERCC2	ERCC3	ERCC4					
ETV4	EXT1	EXT2	EZH2	FANCA					
FBXW7	FGFR1	FGFR2	FGFR3	FGFR4					

Complete list of variants (73)

Gene	Drugs related to gene	Cat	Variant frequency	CDNA variant	Animo acid variant	Biological impact		Therapeutical impact	Medically actionable incidental findings	Drugs related to your patient
CMPK1	0	SNV	80%	c.240G>T	p.Q80H	Probably Polymorphism	●	☰	No	0
PDE4DIP	0	SNV	24%	c.5180T>C	p.L1727P	Unknown	●	☰	No	0
PDE4DIP	0	SNV	12%	c.3664A>G	p.K1222E	Probably Polymorphism	●	☰	No	0
PDE4DIP	0	SNV	13%	c.622A>G	p.T208A	Probably Polymorphism	●	☰	No	0
PDE4DIP	0	SNV	13%	c.248T>A	p.L83Q	Probably Polymorphism	●	☰	No	0
RNASEL	0	SNV	23%	c.1385G>A	p.R462Q	Unknown	● ●	☰	✓	0
ALK	0	SNV	100%	c.4587C>G	p.D1529E	Probably Polymorphism	●	☰	No	0
LRP1B	0	SNV	84%	c.143A>G	p.Q48R	Probably Polymorphism	●	☰	No	0
FANCD2	13	SNV	25%	c.4356+3C>T	-	Unknown	●	☰	No	3
TGFBR2	0	SNV	24%	c.263 7A>G	-	Probably Polymorphism	●	☰	No	0
GATA2	0	SNV	77%	c.490G>A	p.A164T	Probably	●	☰	No	0

Molecular testing:



Results

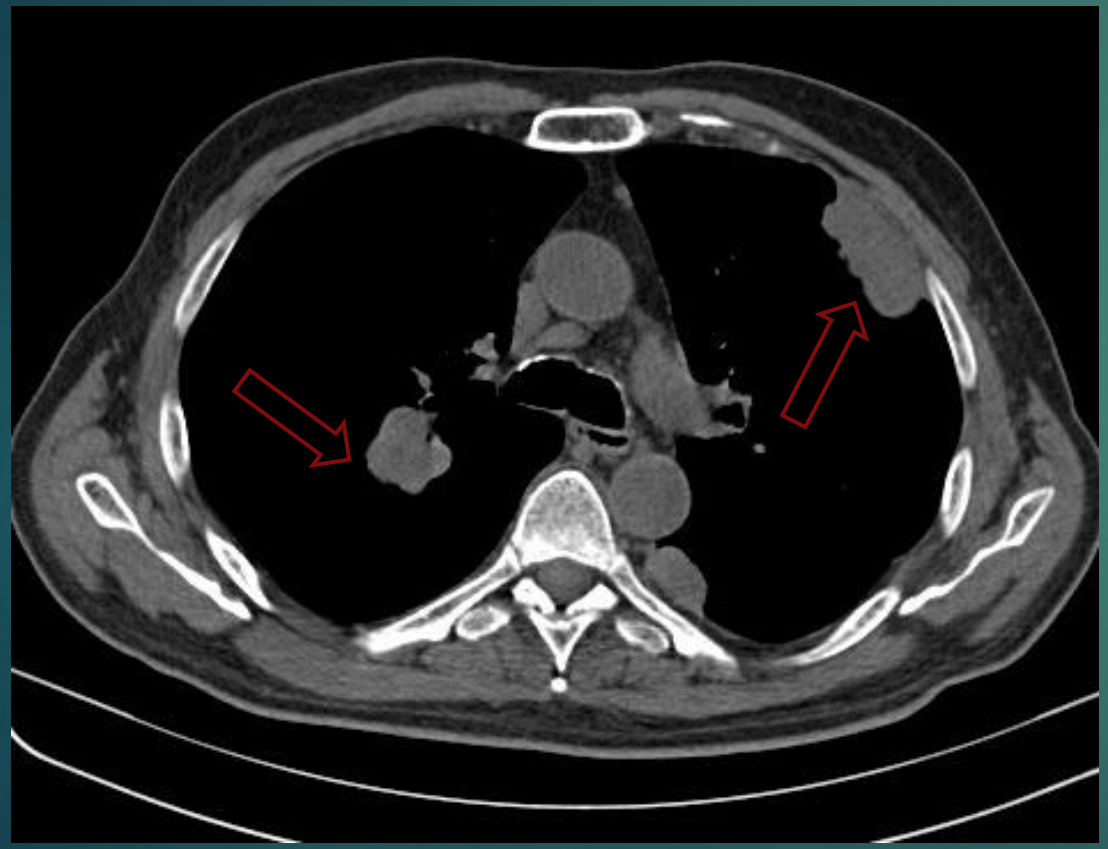
Integrated Biological Review

Treatments associated with Potential Clinical Benefit	Treatments associated with Potential Lack of Clinical Benefit	Treatments associated with Undetermined Clinical Benefit	Treatments associated with toxicity
Gemcitabine (RRM1 IHC)	Platinum based chemotherapy (ERRC1 IHC)		
Anthracycline based chemotherapy (TOP2A IHC)	5-FU based chemotherapy (TS IHC)		
Angiogenesis inhibitors (VEGFR2 IHC)	KIT inhibitors (cKIT IHC)		
	Taxane based chemotherapy (TUBB3 IHC)		
	alkylating agent (MGMT)		
	PD-1/PD-L1 inhibitors (PD-L1 & CD8 IHCs)		

Et maintenant?

- Après les résultats sont discutés au sein du Molecular Tumor Board et il a été décidé de le mettre sous un médicament antiangiogénique qu'on n'aurait jamais utilisé sinon…

Exemple d'un patient réel



10/2015

3/2016

Conclusion

- La révolution moléculaire est en route depuis longtemps en médecine
- Afin de pouvoir faire profiter de tous les patients le plus vite possible de cette révolution il nous faut de l'aide…
- L'intelligence artificielle va être et est déjà omniprésente en science et va se répandre rapidement en médecine
- La révolution numérique a atteint l'Oncologie !!!

Merci !