



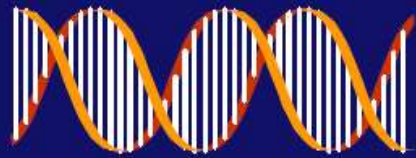
SKML Her-2-neu

Bart de Vries

Her-2-neu

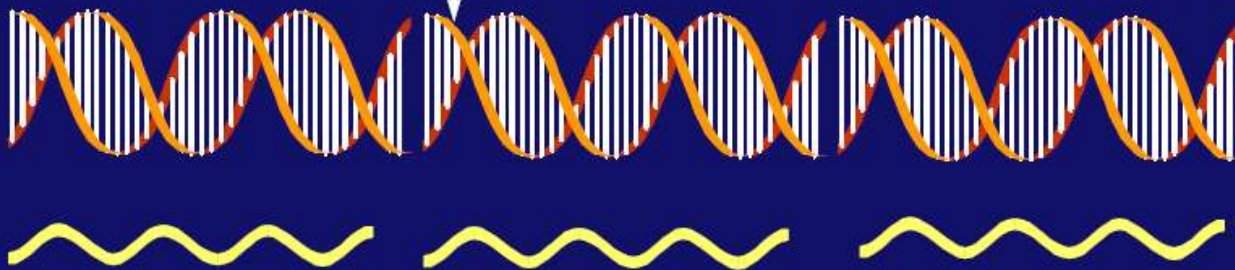
- Introductie
- Stand van zaken
 - Terugkoppeling Her-2-neu IHC / ISH rondzending

HER2 gene amplification

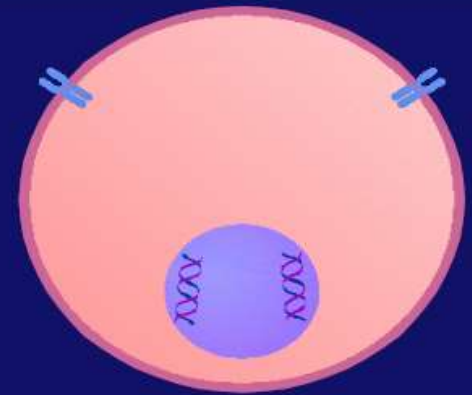


HER2 mRNA

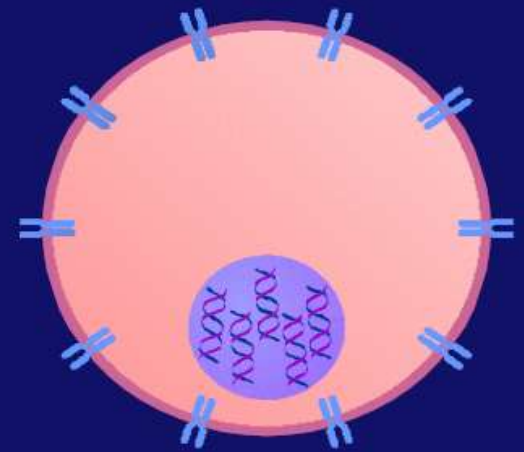
over-replication
 + selection of cells
 with growth advantage



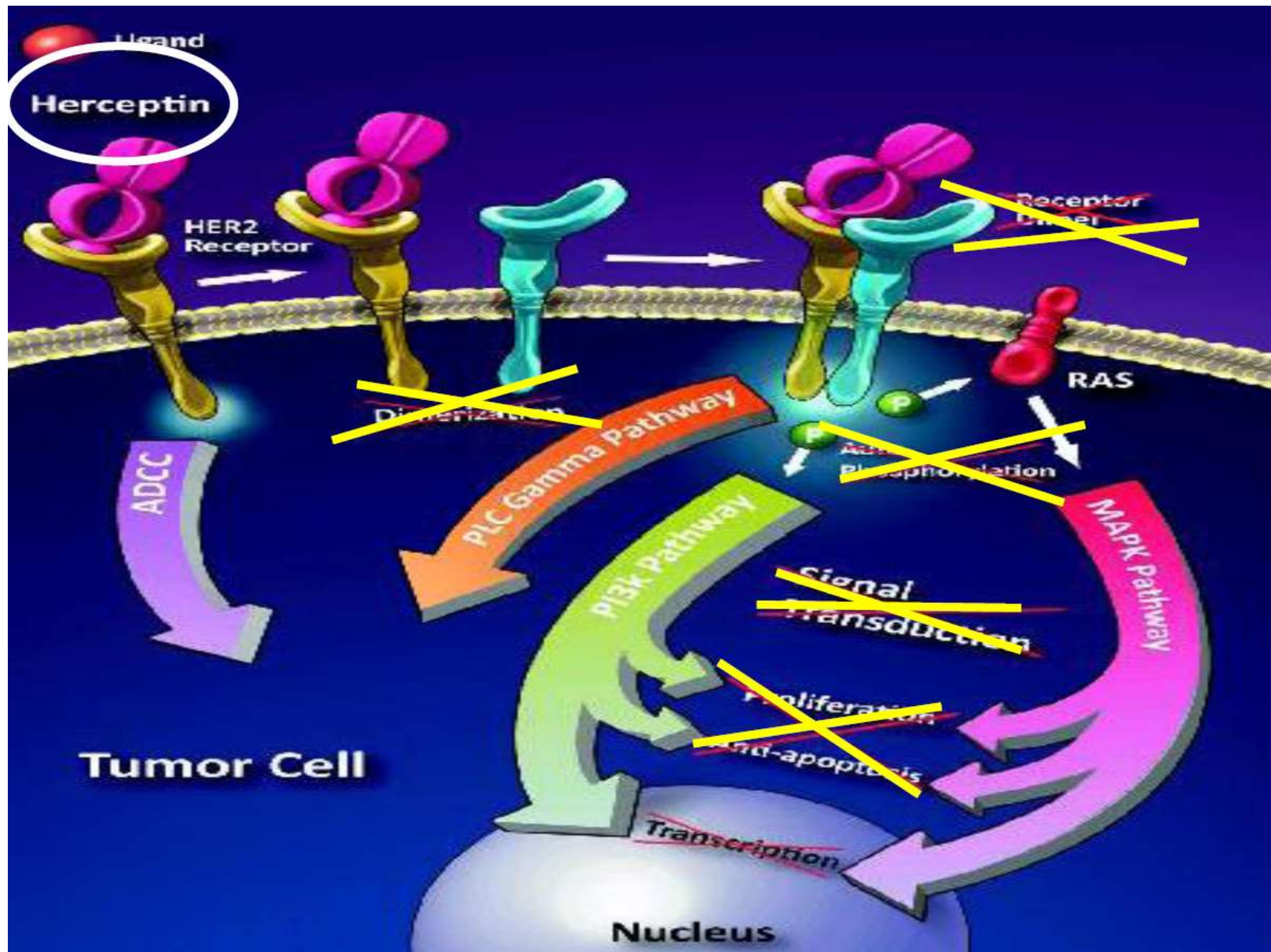
HER2 mRNA



HER2 protein
 normal amount



HER2 protein
 elevated amount



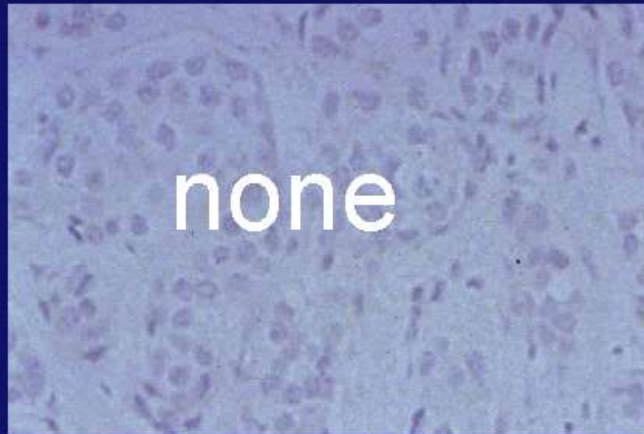
Belang juiste HER2 status

- Een fout-positieve uitslag kan leiden tot een onnodige (dure) therapie met alleen bijwerkingen
- Bij een fout-negatieve uitslag wordt de patiënt een potentieel gunstige therapie onthouden
- Testmethode?
 - IHC
 - FISH, BRISH, SISH, CISH
 - MLPA

HER2-IHC in Breast cancer

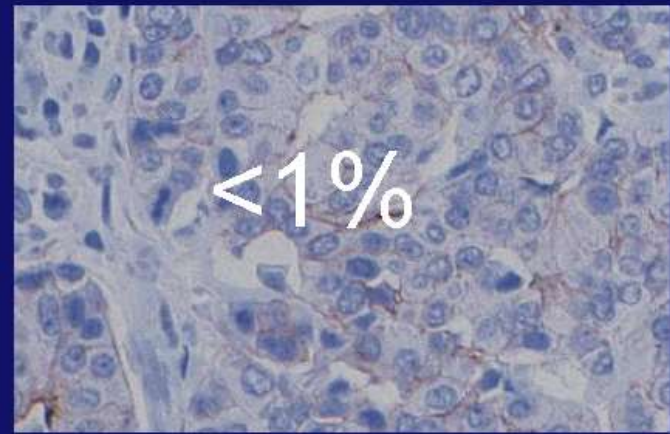
- **IHC 0** (no staining or staining in <10% of tumor cells, negative),
- **IHC 1+** (faint/barely perceptible incomplete membrane staining in >10% of tumor cells, negative),
- **IHC 2+** (weak to moderate complete membrane staining in >10% of tumor cells, equivocal)
- **IHC 3+** (strong complete membrane staining in >10% (until 2007) or >30% (2007–now) of tumor cells)

What % of HER2 amplified cases can be expected?



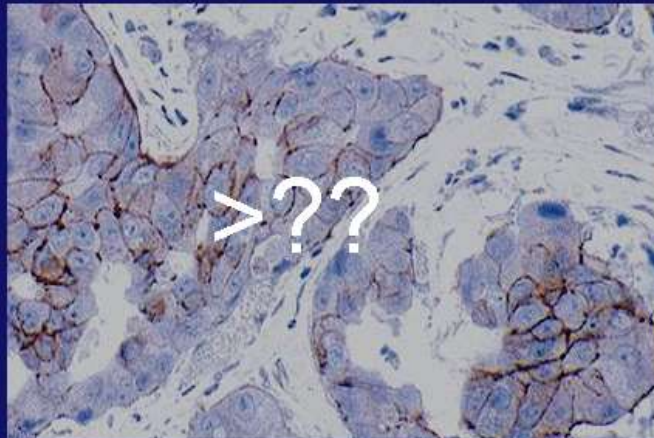
none

0 (negative)



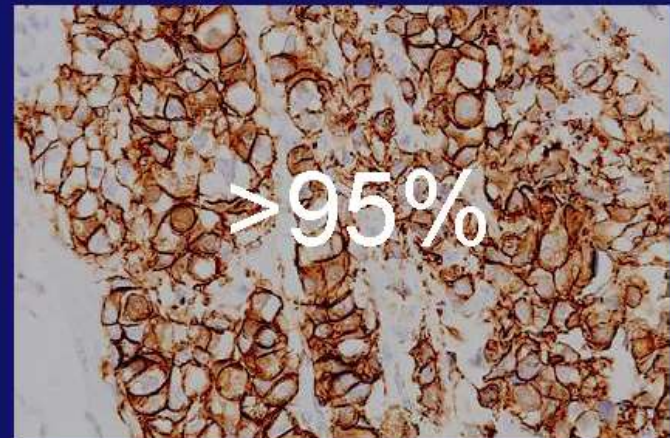
<1%

1+ (negative)



>??

2+ (equivocal)

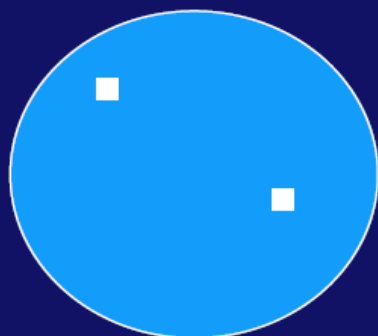


>95%

3+ (positive)

HER2 testing in Breast cancer (ISH-mono)

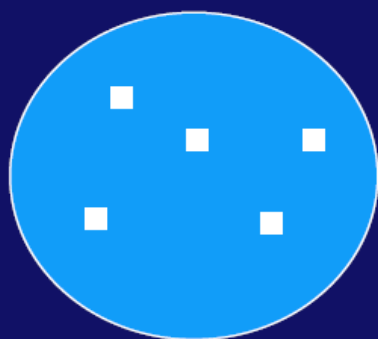
Small cluster of 'large' spot?



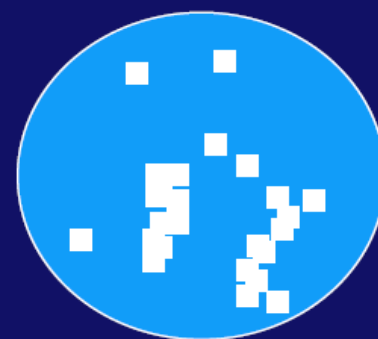
Her2 (normal)



Her2 (amplified, 6-10)

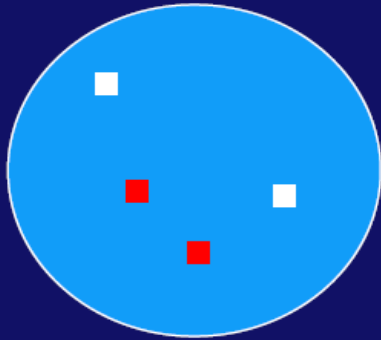


Her2 (equivocal, 3-5)

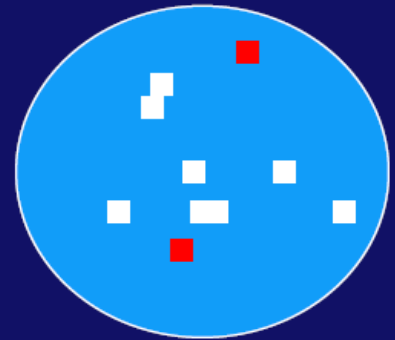


Her2 (amplified >10)

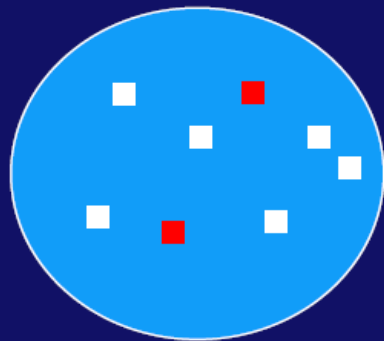
HER2 testing in Breast cancer (ISH-duo)



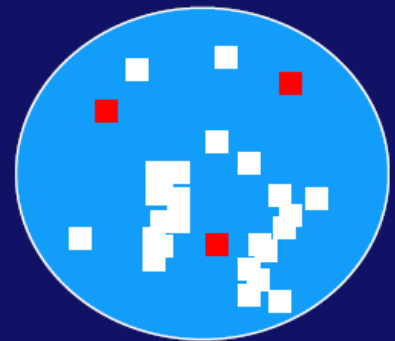
Her2 (normal, <1.8)



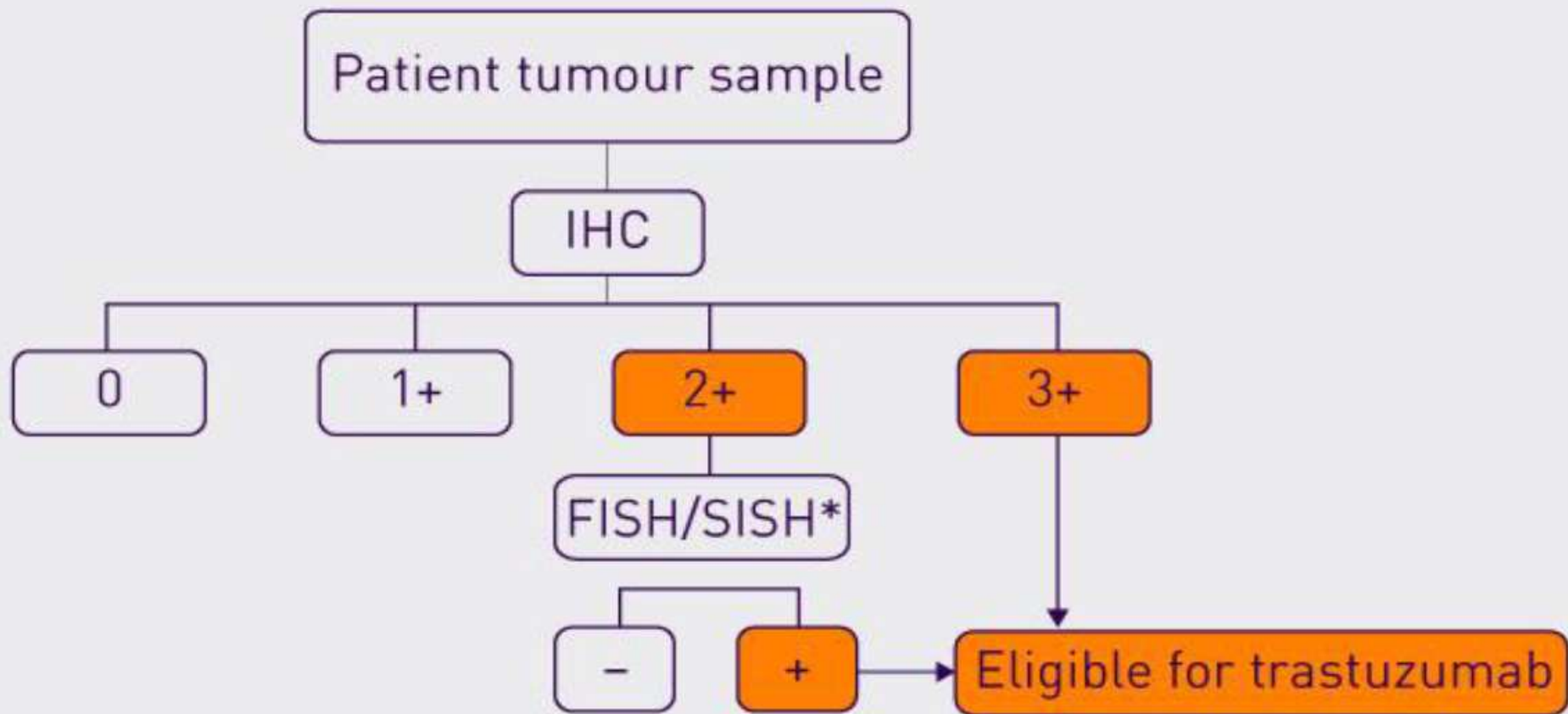
Her2 (amplified, >2.2)



Her2 (equivocal, $1.8-2.2$)



Her2 (amplified >2.2)



SKML rondzending

Overzicht op glaasje:

H	G	E	C	A	matrand
		F	D	B	

De toegestuurde weefsels bij deze ronde zijn:

A = Lever

B = Mamma I = 0 / 1+

C = Mamma II = 0 / 1+

D = Mamma III = 2+ geen amplificatie

E = Mamma IV = 2+ amplificatie

F = Mamma V = 2+ amplificatie

G = Mamma VI = 3+ amplificatie

H = Mamma VII = 3+ amplificatie

SKML Her-2-neu

- 37 laboratoria (31 IHC, 29 ISH)
- 2014.1 : IHC (-> ISH?)
- 2014.2 : ISH

SKML Her-2-neu

IHC:

31 x 7 = 217 patienten

Foutief resultaat (vals negatief): **20 (9%)**

correctie (1+ toch FISH) : 15 (7%)

ISH:

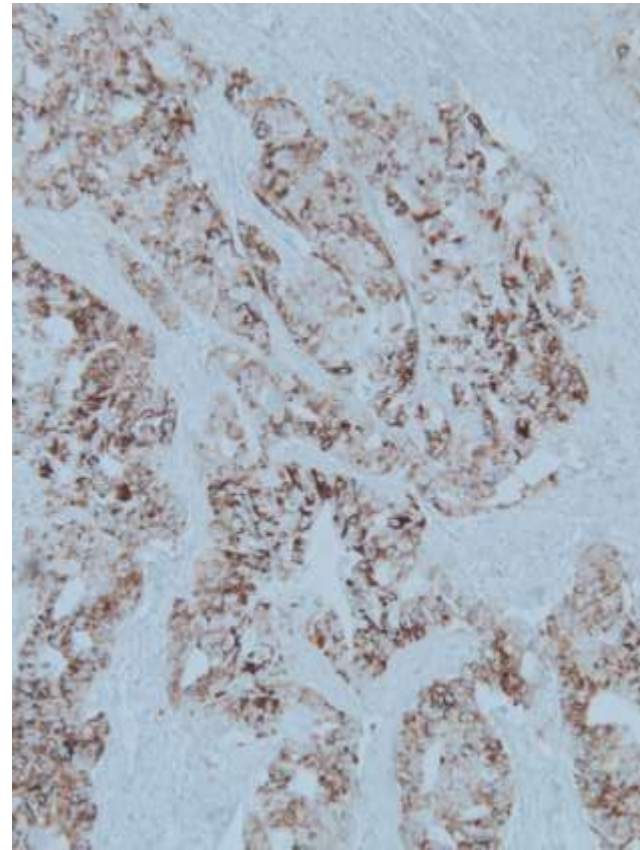
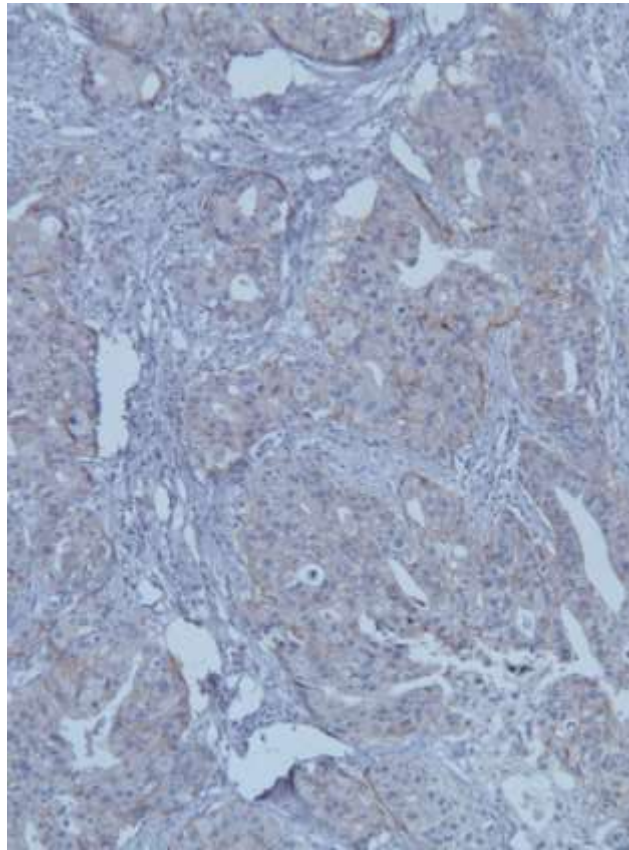
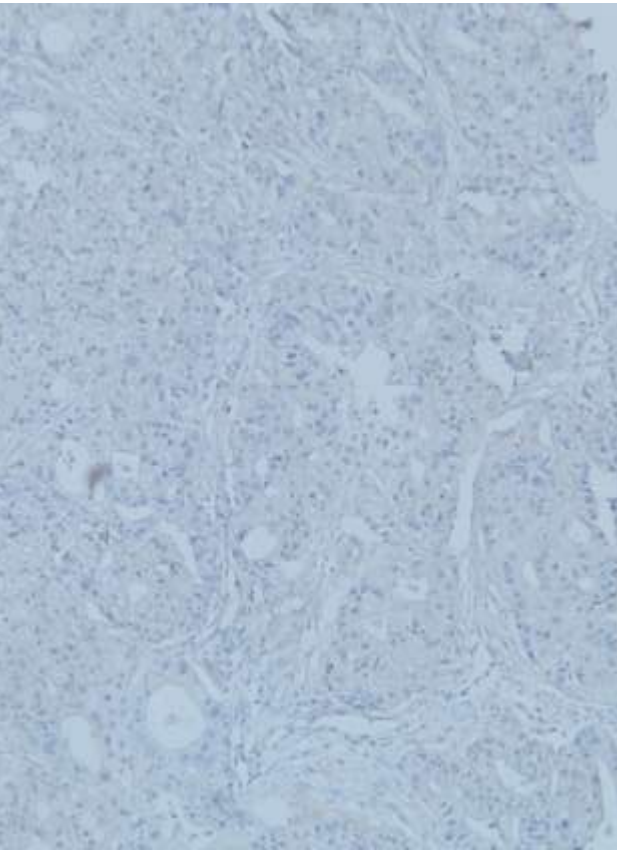
29 x 7 = 203 patienten

Foutief resultaat (vals positief): 1 (0,5%)

(vals negatief): 3 (**1,5%**)



IHC

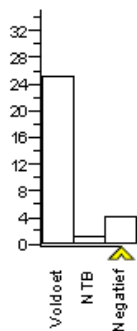


IHC

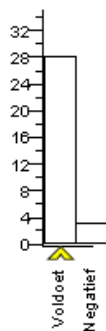
Her2 IHC

Her2 kleuring voldoet

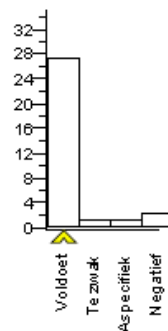
2014.1 A



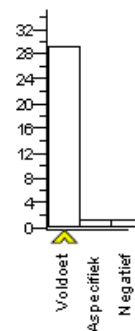
2014.1 B



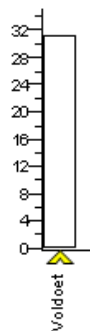
2014.1 C



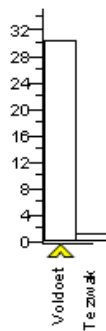
2014.1 D



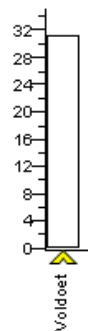
2014.1 E



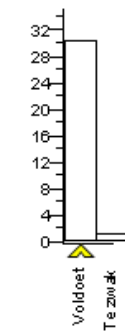
2014.1 F



2014.1 G



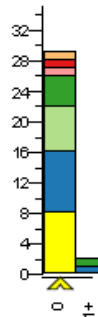
2014.1 H



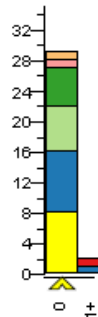
IHC

Her2 IHC score

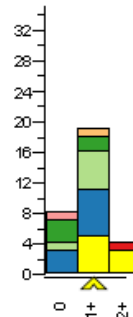
2014.1 B



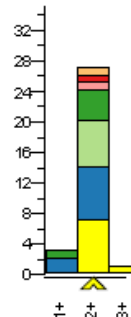
2014.1 C



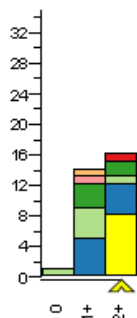
2014.1 D



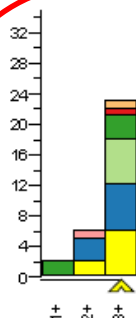
2014.1 E



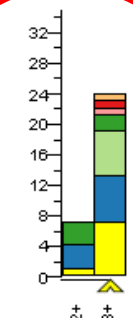
2014.1 F



2014.1 G



2014.1 H



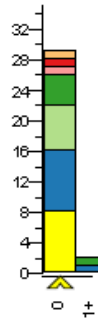
Legenda

SP3 geconcentreerd	Polyclonaal	4B5 ready to use	Anders	SP3 ready to use
CB11 geconcentreerd	3B5 ready to use			

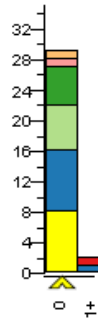
IHC

Her2 IHC score

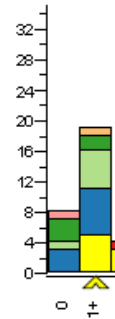
2014.1 B



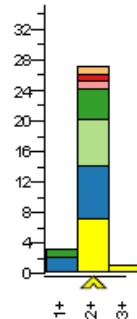
2014.1 C



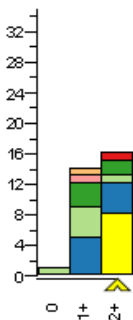
2014.1 D



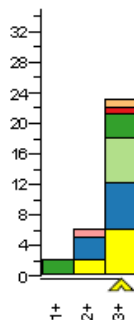
2014.1 E



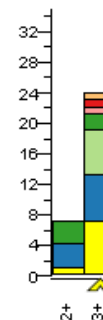
2014.1 F



2014.1 G



2014.1 H



Legenda

SP3 geconcentreerd	Polyclonaal	4B5 ready to use	Anders	SP3 ready to use
CB11 geconcentreerd	3B5 ready to use			

IHC 0/1+ : 18% ISH amplificatie !!!

IHC 1+ : 45% ISH amplificatie !!!

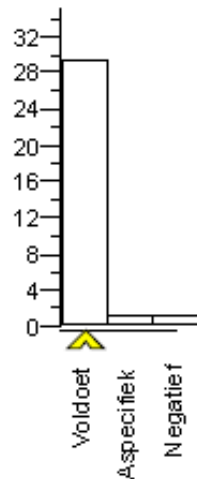
SKML IHC core D

Core D : IHC 2+, ISH negatief

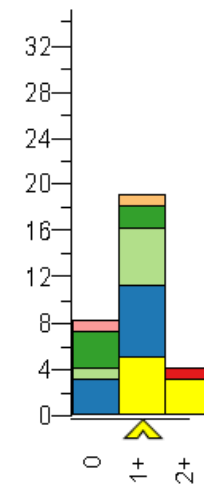
IHC score			
0	1	0/1	2
25.8%	61.3%	68.8%	12.9%

ISH ?	Ja	
		35.5%

2014.1 D



2014.1 D



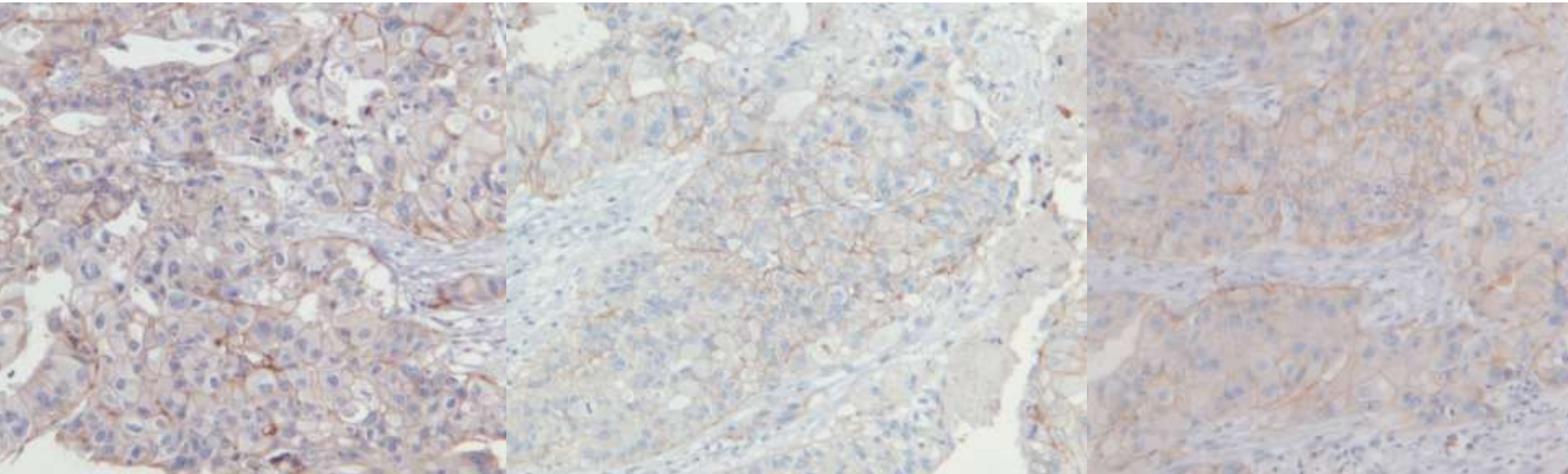
SKML IHC core D



4B5 en 3B5

Comments

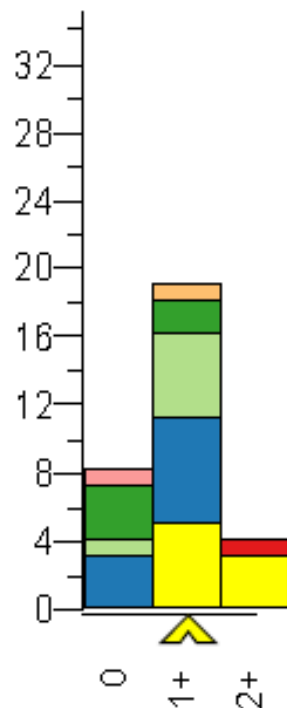
Bij weefsel D zien wij heel veel korreling in het cytoplasma
Coupe D: veel cytoplasmatische kleuring, ISH overwegen



SKML IHC core D

Core D : IHC **2+**, ISH **negatief**

2014.1 D

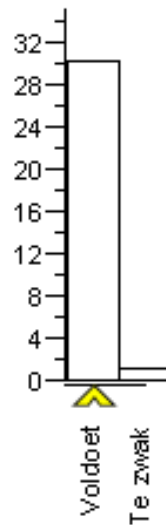


SKML IHC core F

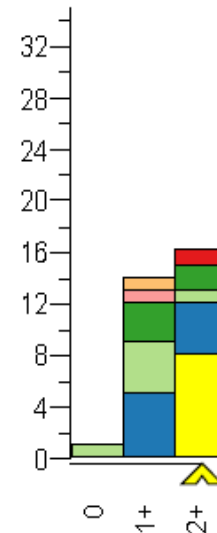
Core F : IHC **2+**, ISH **positief**

IHC			
0	1	0/1	2
3.2%	45.2%	48.4%	51.6%
ISH ?	ja		61.3%

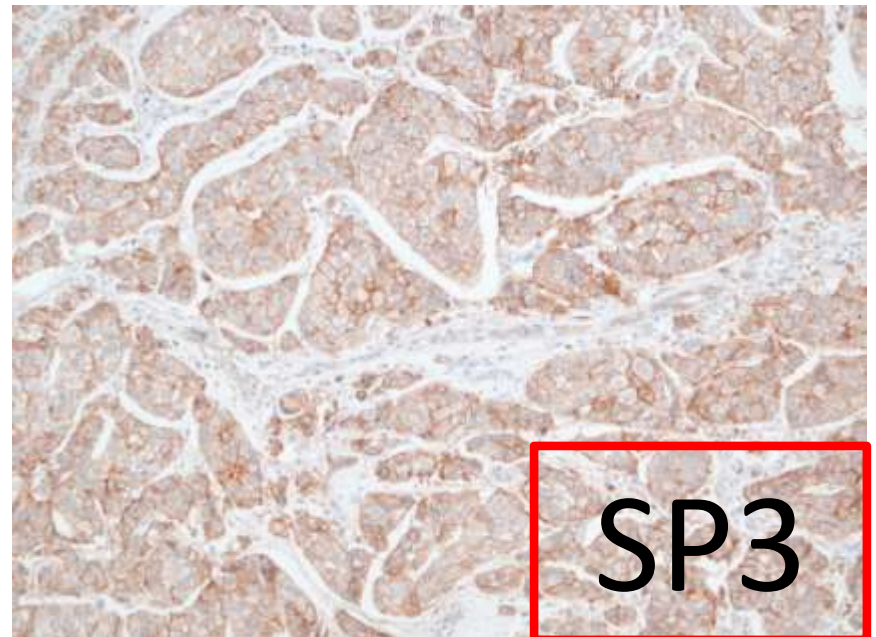
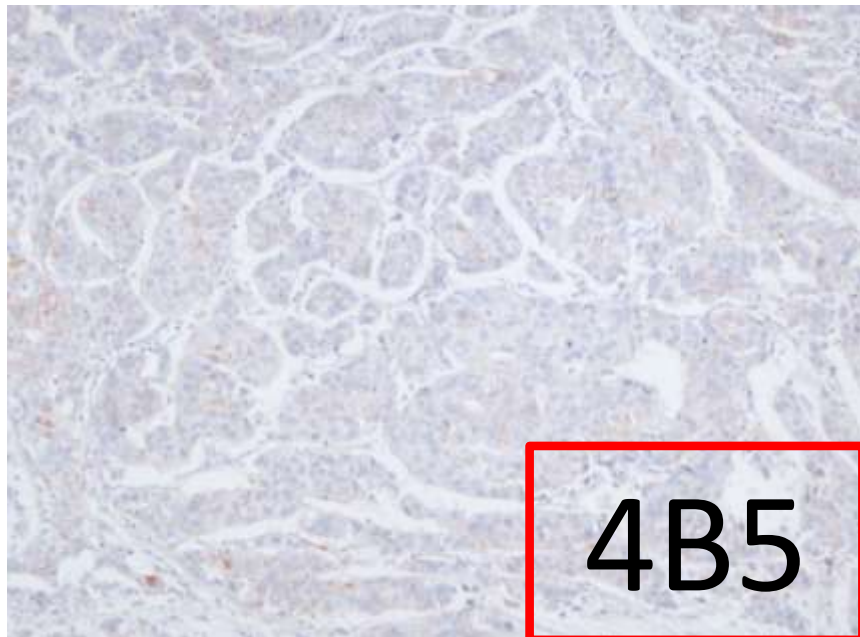
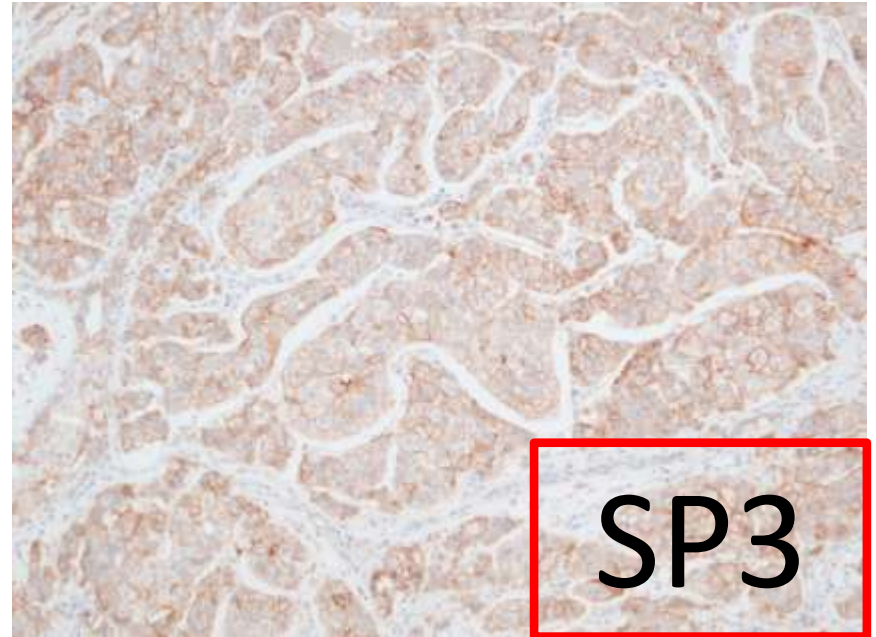
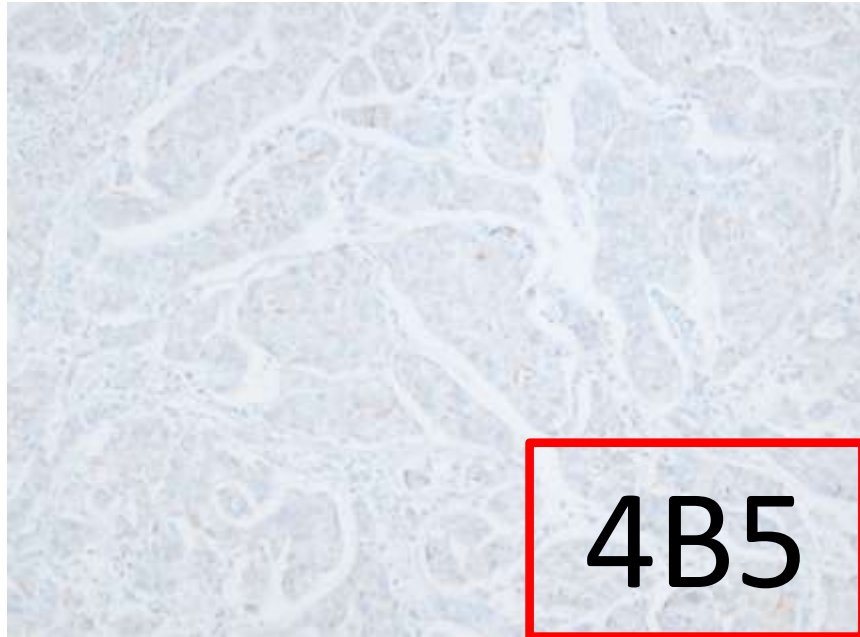
2014.1 F



2014.1 F

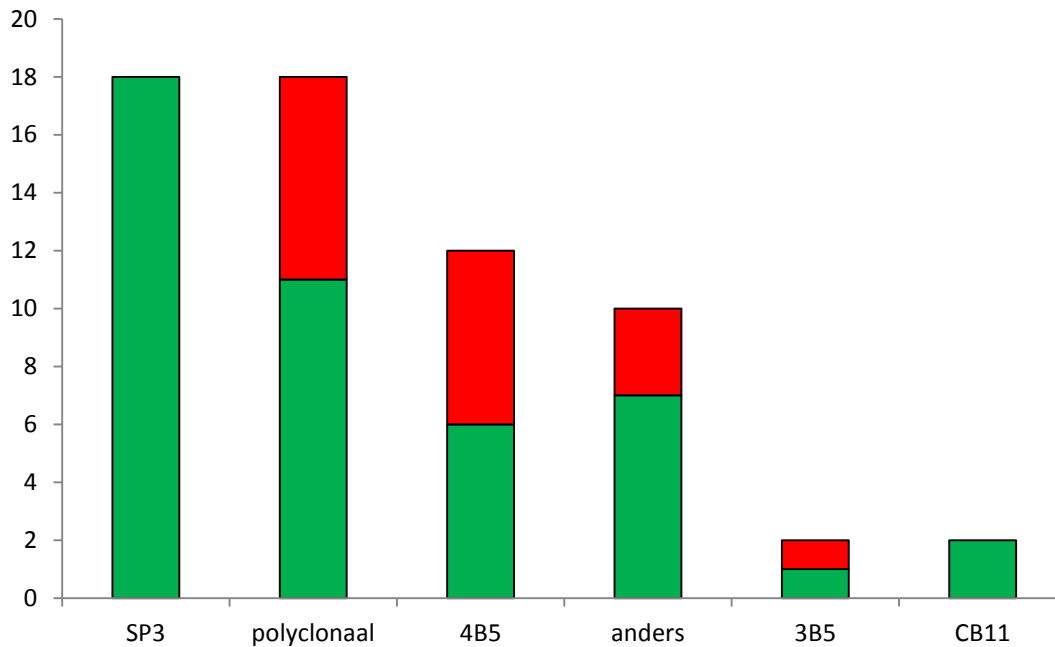


SKML IHC core F



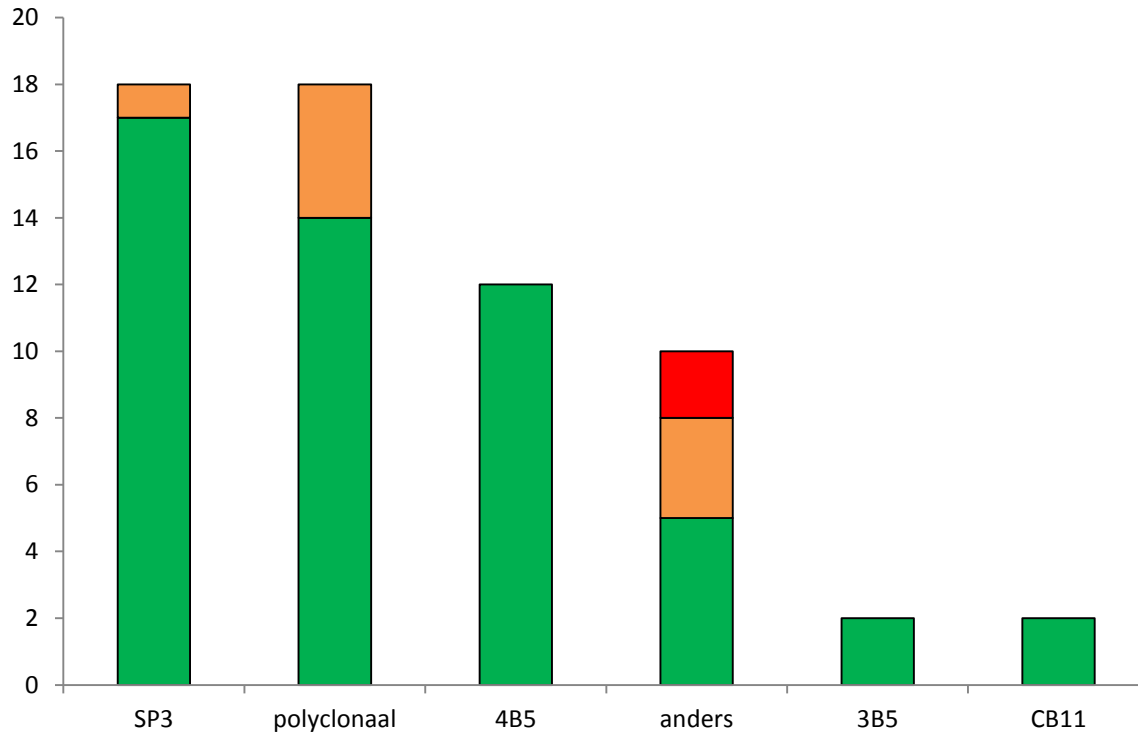
Resultaten per Ab

IHC 2+ geamplificeerd:



Resultaten per Ab

IHC 3+ (geamplificeerd):



Welk antilichaam ?

Modern Pathology (2009) 22, 879-886
© 2009 USCAP, Inc. All rights reserved 0893-3952/09 \$32.00
www.modernpathology.org

Validation of the 4B5 rabbit monoclonal antibody in determining Her2/neu status in breast cancer

Bert van der Vegt¹, Geertruida H de Bock², Joost Bart¹, Nick G Zwart¹ and Jelle Wesseling^{1,3}

Dekker et al. Breast Cancer Research 2012, 14:R93
<http://breast-cancer-research.com/content/14/3/R93>

RESEARCH ARTICLE

Determining sensitivity and specificity of HER2 testing in breast cancer using a tissue microarray approach

Tim JA Dekker^{1,2}, Susan Ter Borg³, Gerrit KJ Hooijer³, Sybren L Meijer³, Jelle Wesseling⁴, James E Boers⁵, Ed Schuurings⁶, Jos Bart⁶, Joost van Gorp⁷, Wilma E Mesker², Judith R Kroep¹, Vincent THBM Smit⁸ and Marc J van de Vijver^{3*}

Original article

Downloaded from <http://jcp.bmj.com/> on June 15, 2015 - Published by group.bmj.com

The Reliability of Rabbit Monoclonal Antibodies in the Immunohistochemical Assessment of Estrogen Receptors, Progesterone Receptors, and HER2 in Human Breast Carcinomas

Anthony Rhodes, PhD,¹ Julia Sarson, MSc,² Emma E. Assam, MSc,¹ Sarah J.R. D'Cruz,¹ Edward C. Cribb, BSc (Hons),¹ and Andrew Parker, FRCPA³

Comparative analysis of six different antibodies against Her2 including the novel rabbit monoclonal antibody (SP3) and chromogenic in situ hybridisation in breast carcinomas

C B Nunes,¹ R M Rocha,¹ J S Reis-Filho,² M B Lambros,² G F S Rocha,¹ F S F Sanches,¹ F N Oliveira,¹ H Gobbi¹

IHC 2014

Foutief resultaat (vals negatief): **20 (9%)**

- IHC 0/1+ : 18% ISH amplificatie !!!
- IHC 1+ : 45% ISH amplificatie !!!

IHC 2013:

Foutief resultaat (vals negatief): **29 (13%)**

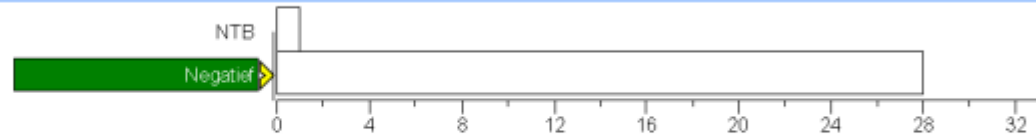


ISH samples B-D

Monster : 2014.2 B

Score

Beoordeling voor Her2 amplificatie in monster B (mamma 1):

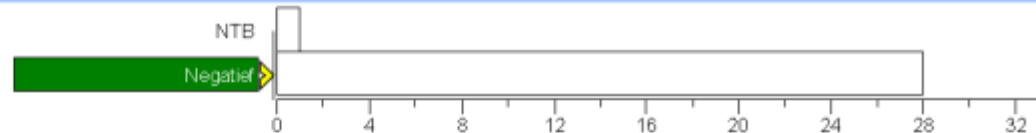


2

Monster : 2014.2 C

Score

Beoordeling voor Her2 amplificatie in monster C (mamma 2):

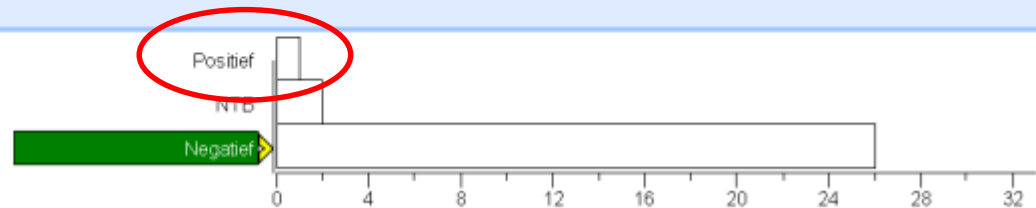


2

Monster : 2014.2 D

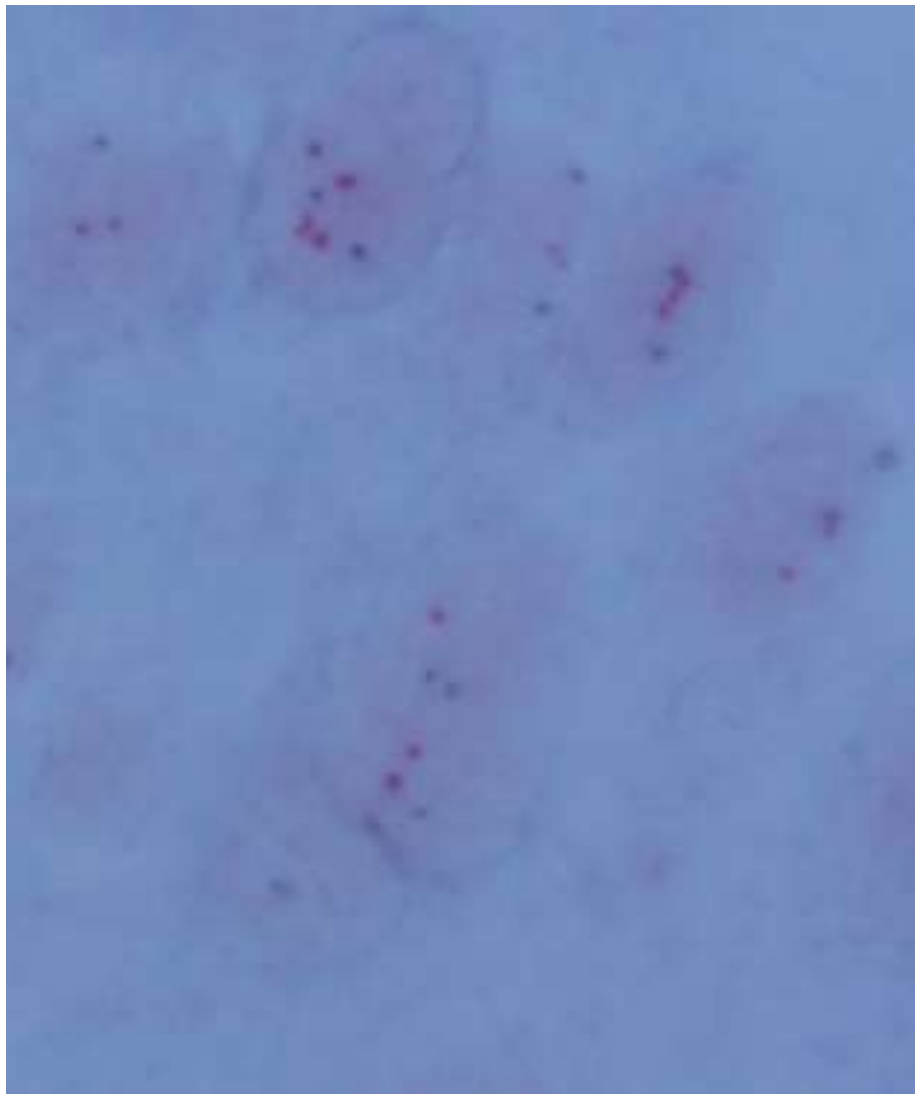
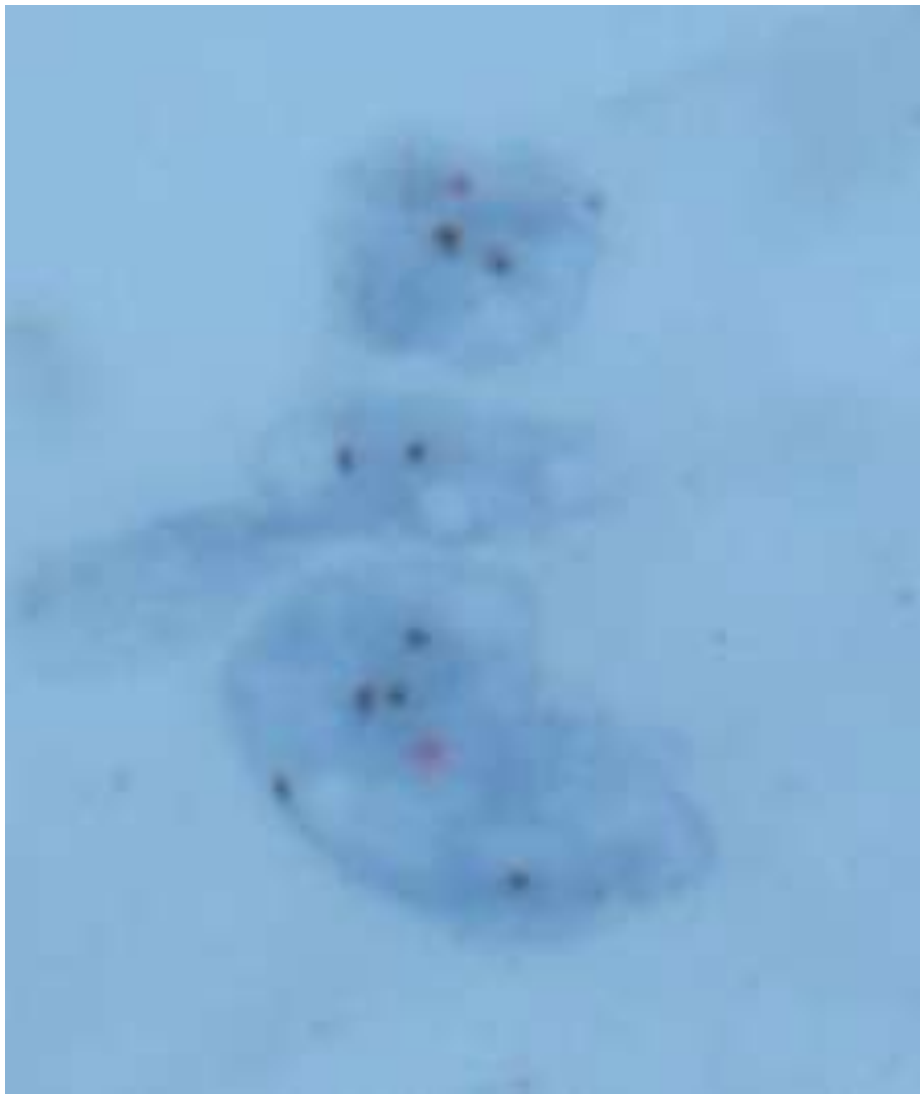
Score

Beoordeling voor Her2 amplificatie in monster D (mamma 3):



2

weinig cep 17- signaal t.o.v. Her2Neu, dus zwakke rode aankleuring.

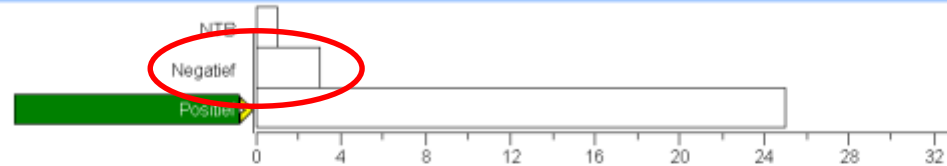


ISH samples E-H

Monster : 2014.2 E

Score

Beoordeling voor Her2 amplificatie in monster E (mamma 4):

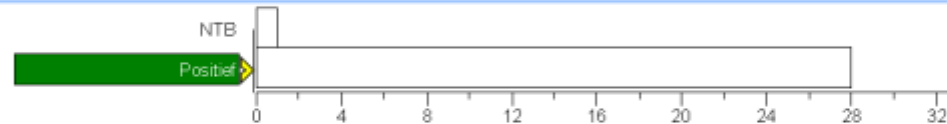


2

Monster : 2014.2 F

Score

Beoordeling voor Her2 amplificatie in monster F (mamma 5):

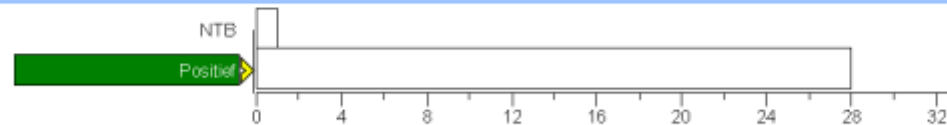


2

Monster : 2014.2 G

Score

Beoordeling voor Her2 amplificatie in monster G (mamma 6):

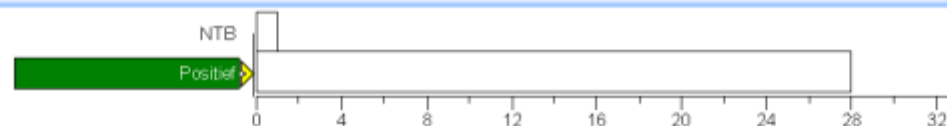


2

Monster : 2014.2 H

Score

Beoordeling voor Her2 amplificatie in monster H (mamma 7):

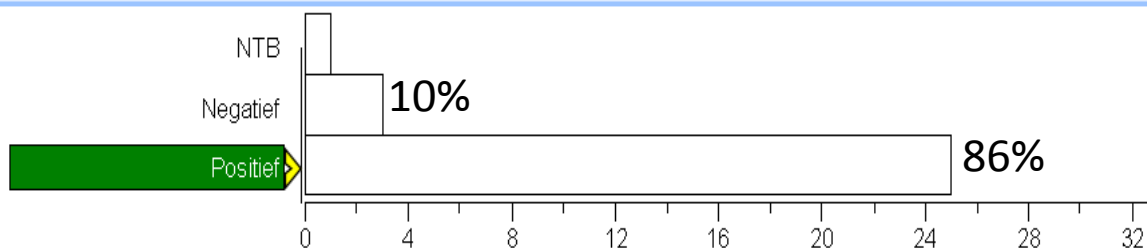


2

ISH core E

Monster : 2014.2 E

Beoordeling voor Her2 amplificatie in monster
E (mamma 4):



ISH score

1. Her2/Chr17 1,8-2,2 (equivocal)
2. Kopie/kern 5,1-6,0 (equivocal)
3. Kopie/kern 5,1-6,0 (equivocal)

Comments

Zwakke signalen CHR. 17, moeilijk te beoordelen
Herhalen met FISH techniek
FISH aanvragen

Totaal score ISH

Aantal deelnemers	Totale score
24	14
3	11
1	9

SKML Her-2-neu

IHC:

31 x 7 = 217 patienten

Foutief resultaat (vals negatief): **20 (9%)**

correctie (1+ toch FISH) : 15 (7%)

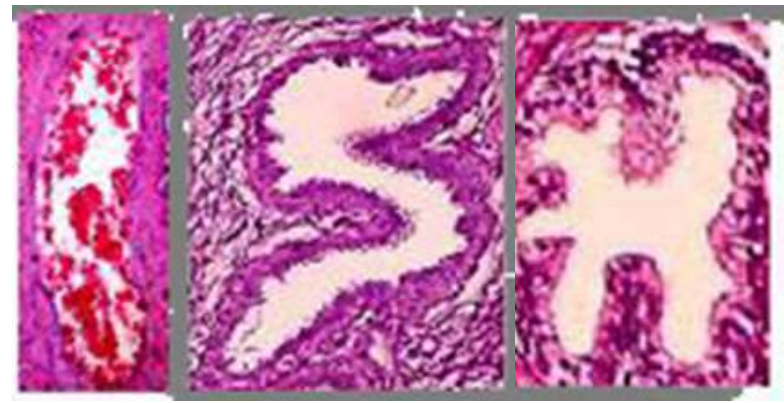
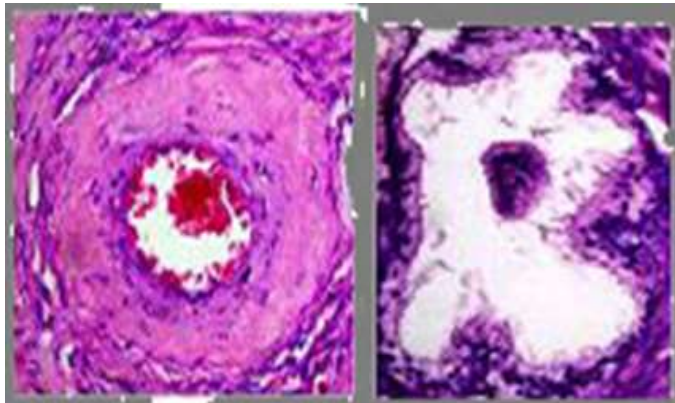
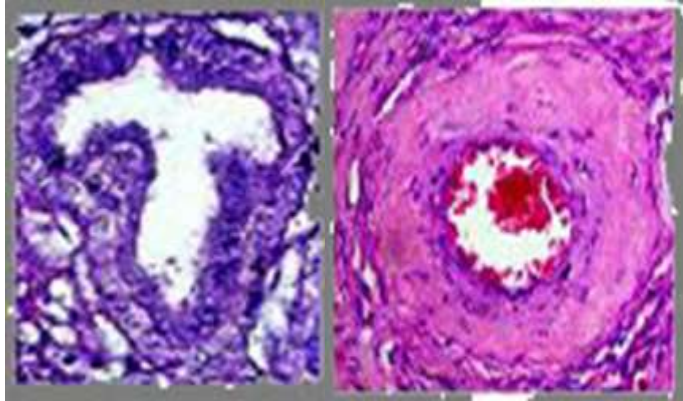
ISH:

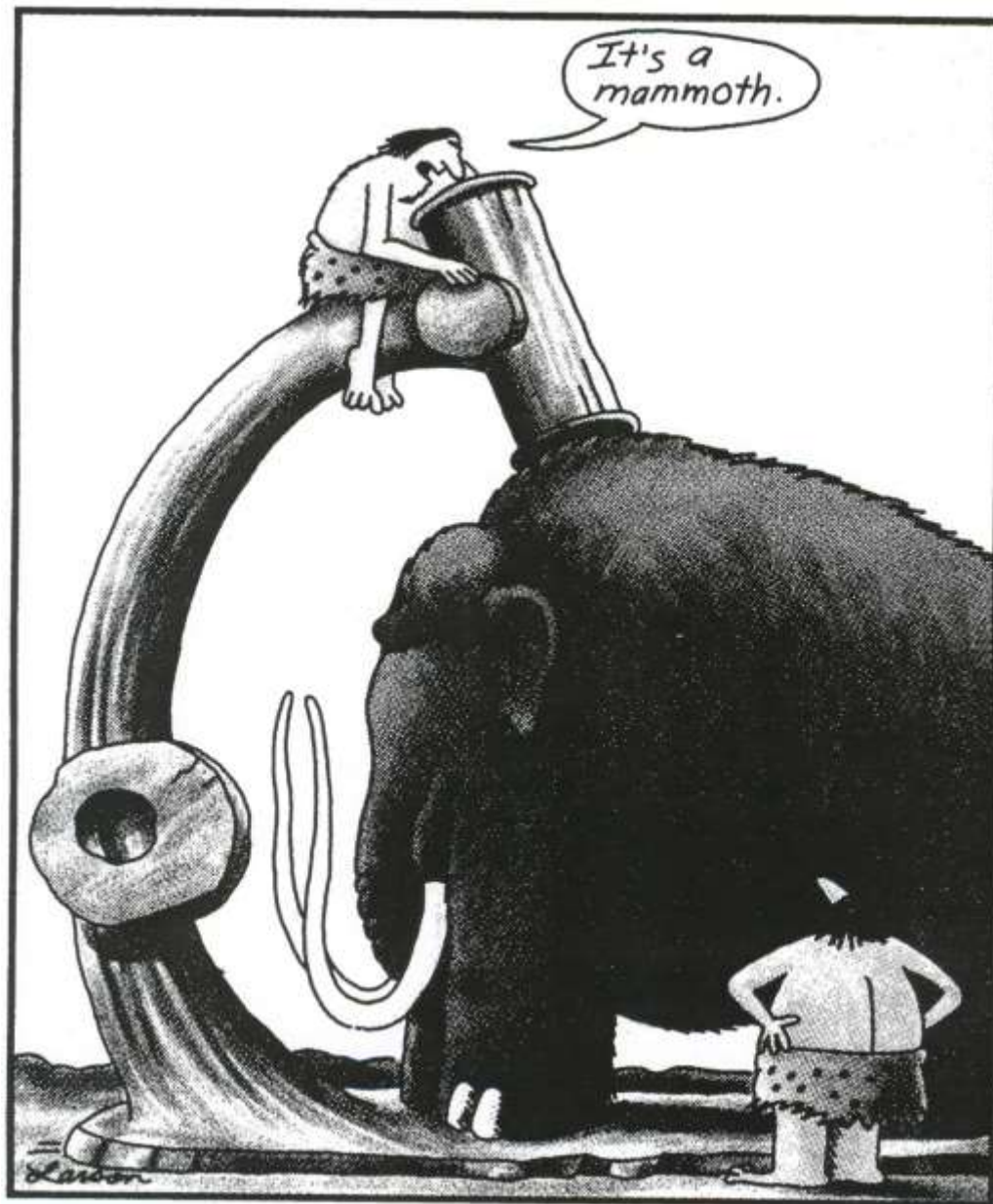
29 x 7 = 203 patienten

Foutief resultaat (vals positief): 1 (0,5%)

(vals negatief): 3 (**1,5%**)

maar: 3x equivocal (2x advies FISH)



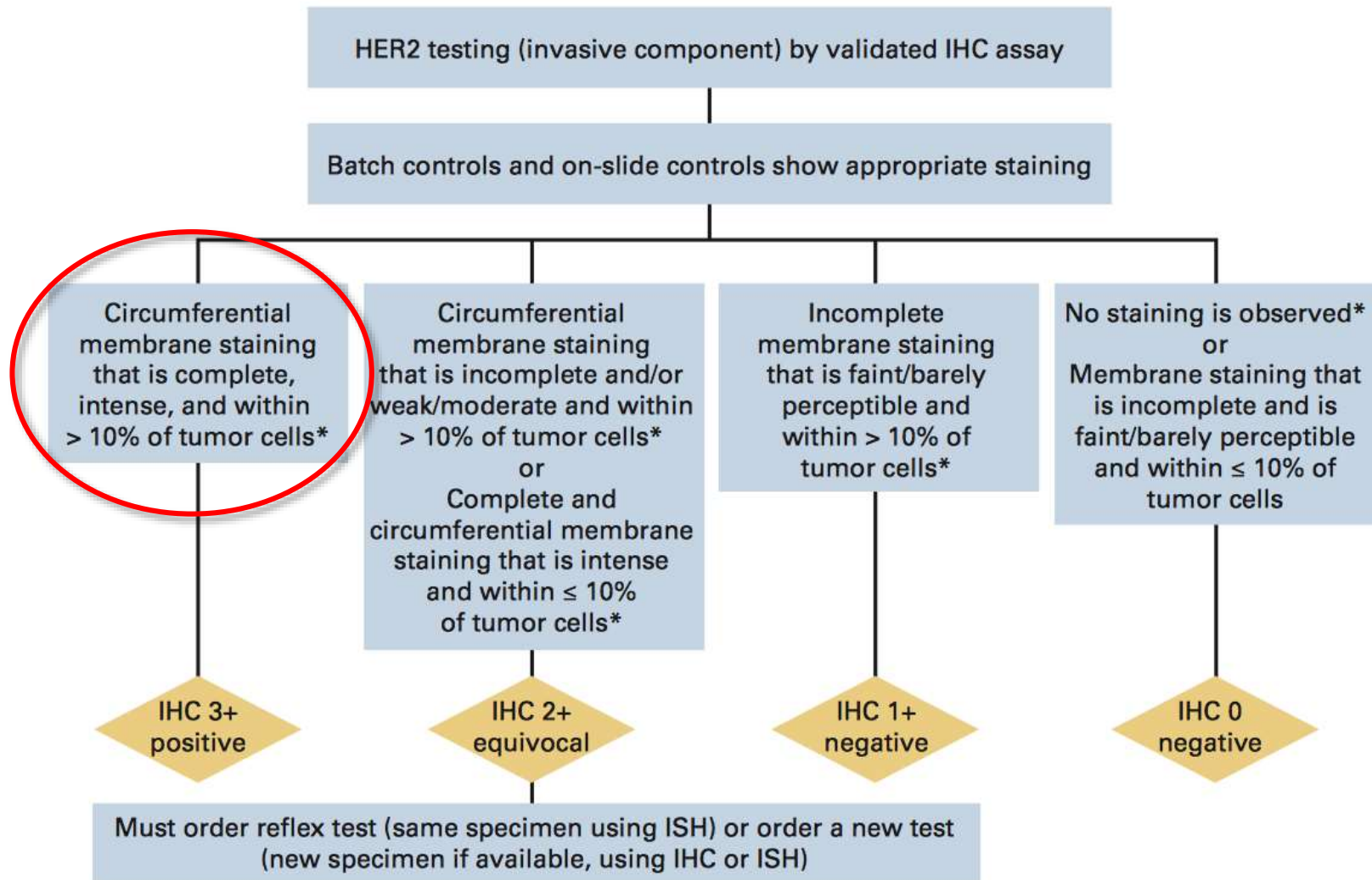


Early microscopes

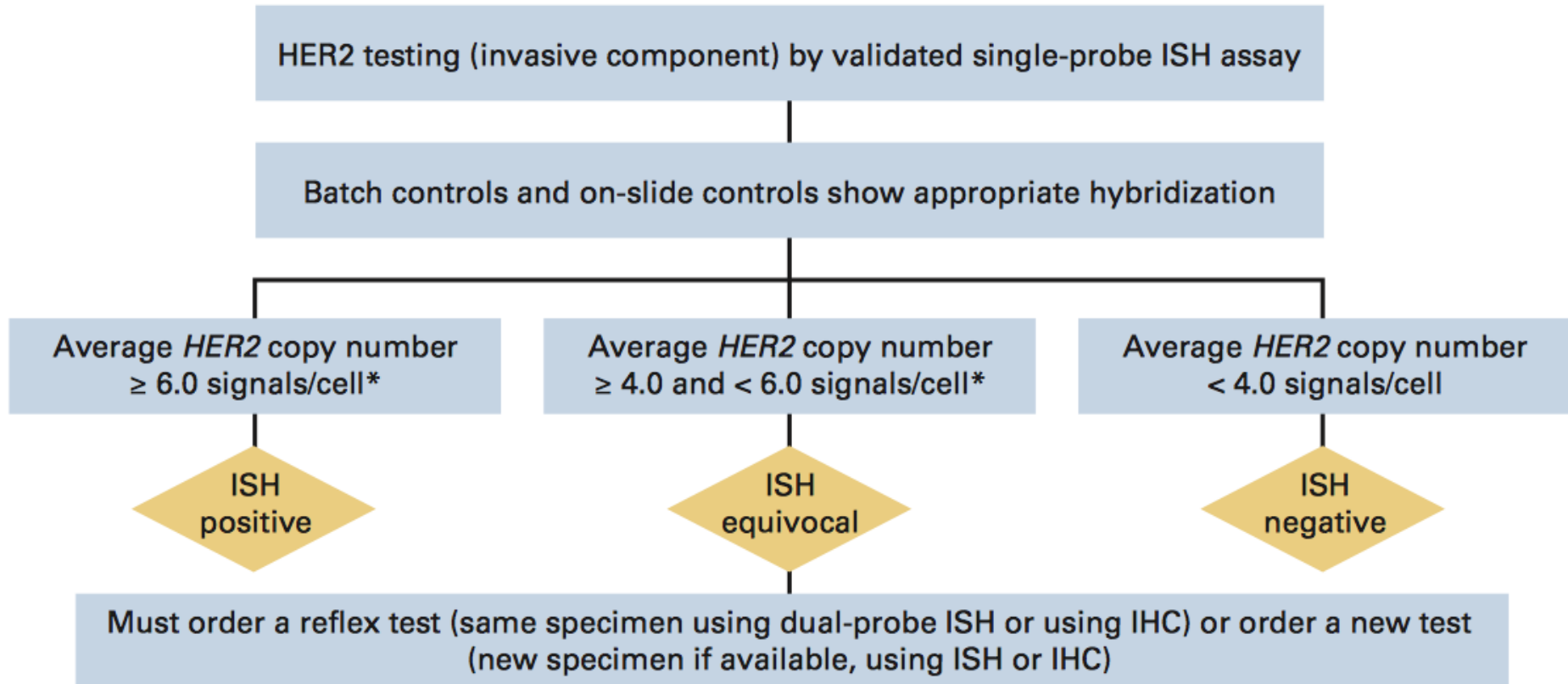
Toekomst perspectief

Nieuwe ASCO / CAP richtlijn 2013

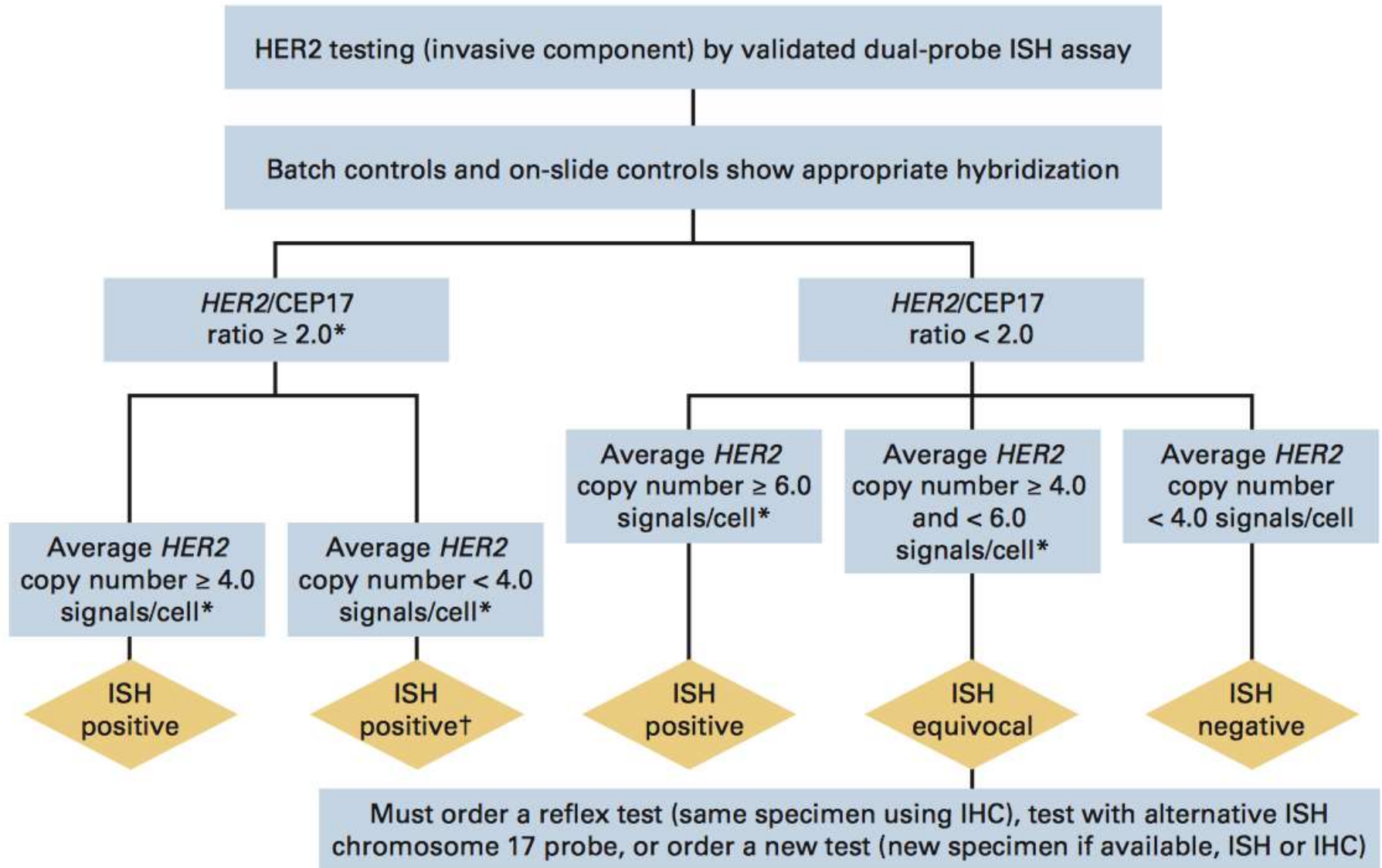
IHC



Single probe ISH



Dual probe ISH



To take home:

Her-2 testing: to treat or not to treat

IHC scoort goed voor 0 en 3+

IHC onder de maat voor 1+ en 2+

ISH scoort goed (uitgezonderd equivocal)

Cave 1+ (en 2+) IHC

Laagdrempelig ISH



Ernst-Jan Speel (MUMC+)
Vincent Smit (LUMC)
Ilonka Stuij (SKML)