

CONNECTION-II

Improving clinical management of colon cancer through CONNECTION, a nation-wide Colon Cancer Registry and Stratification effort

Robert Coebergh van den Braak

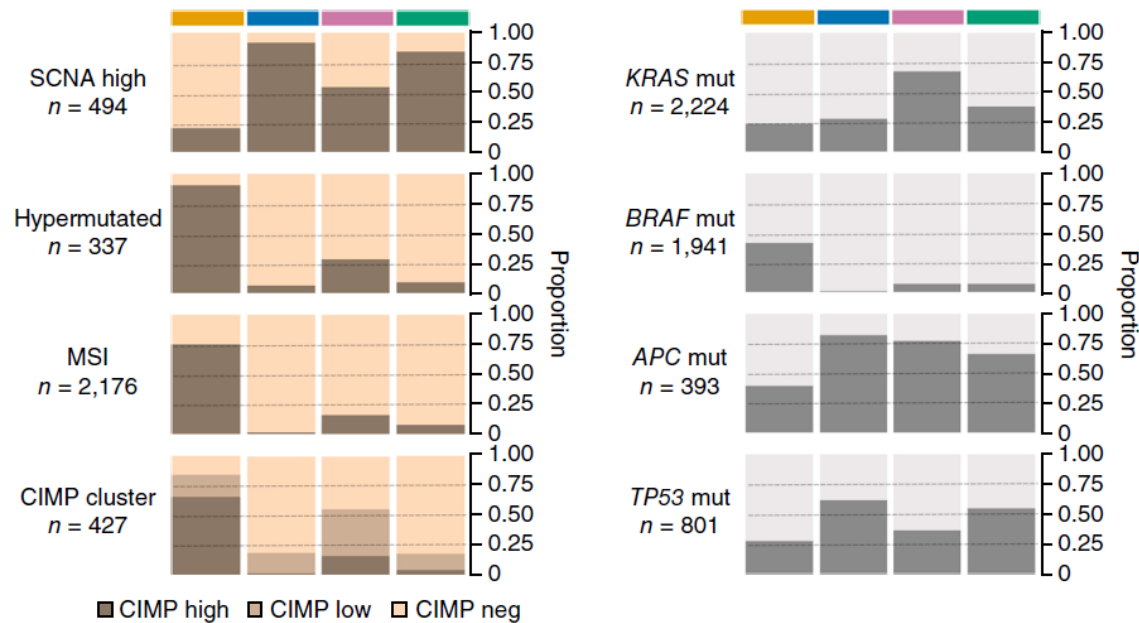
Arts-onderzoeker Erasmus MC, namens het CONNECTION-consortium

The consensus molecular subtypes of colorectal cancer

Justin Guinney^{1,21}, Rodrigo Dienstmann^{1,2,21}, Xin Wang^{3,4,21}, Aurélien de Reyniès^{5,21}, Andreas Schlicker^{6,21}, Charlotte Soneson^{7,21}, Laetitia Marisa^{5,21}, Paul Roepman^{8,21}, Gift Nyamundanda^{9,21}, Paolo Angelino⁷, Brian M Bot¹, Jeffrey S Morris¹⁰, Iris M Simon⁸, Sarah Gerster⁷, Evelyn Fessler³, Felipe De Sousa E Melo³, Edoardo Missiaglia⁷, Hena Ramay⁷, David Barras⁷, Krisztian Homicsko¹¹, Dipen Maru¹⁰, Ganiraju C Manyam¹⁰, Bradley Broom¹⁰, Valerie Boige¹², Beatriz Perez-Villamil¹³, Ted Laderas¹, Ramon Salazar¹⁴, Joe W Gray¹⁵, Douglas Hanahan¹¹, Josep Tabernero², Rene Bernards⁶, Stephen H Friend¹, Pierre Laurent-Puig^{16,17,22}, Jan Paul Medema^{3,22}, Anguraj Sadanandam^{9,22}, Lodewyk Wessels^{6,22}, Mauro Delorenzi^{7,18,19,22}, Scott Kopetz^{10,22}, Louis Vermeulen^{3,22} & Sabine Tejpar^{20,22}

CMS1 MSI Immune	CMS2 Canonical	CMS3 Metabolic	CMS4 Mesenchymal
MSI, CIMP high Hypermutation	SCN high	Mixed MSI status SCNA low, CIMP low	SCN high
<i>BRAF</i> mutations		<i>KRAS</i> mutations	
Immune infiltration and activation	WNT and MYC activation	Metabolic deregulation	Stromal infiltration TGF beta activation Angiogenesis

CMS1 MSI Immune	CMS2 Canonical	CMS3 Metabolic	CMS4 Mesenchymal
MSI, CIMP high Hypermutation	SCN high	Mixed MSI status SCNA low, CIMP low	SCN high
<i>BRAF</i> mutations		<i>KRAS</i> mutations	
Immune infiltration and activation	WNT and MYC activation	Metabolic deregulation	Stromal infiltration TGF beta activation Angiogenesis

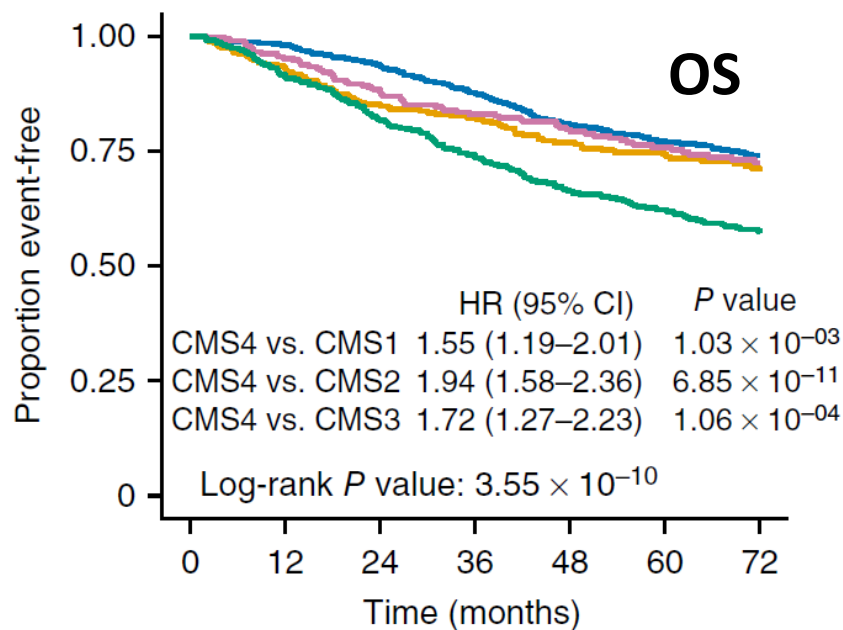


CMS1
MSI Immune

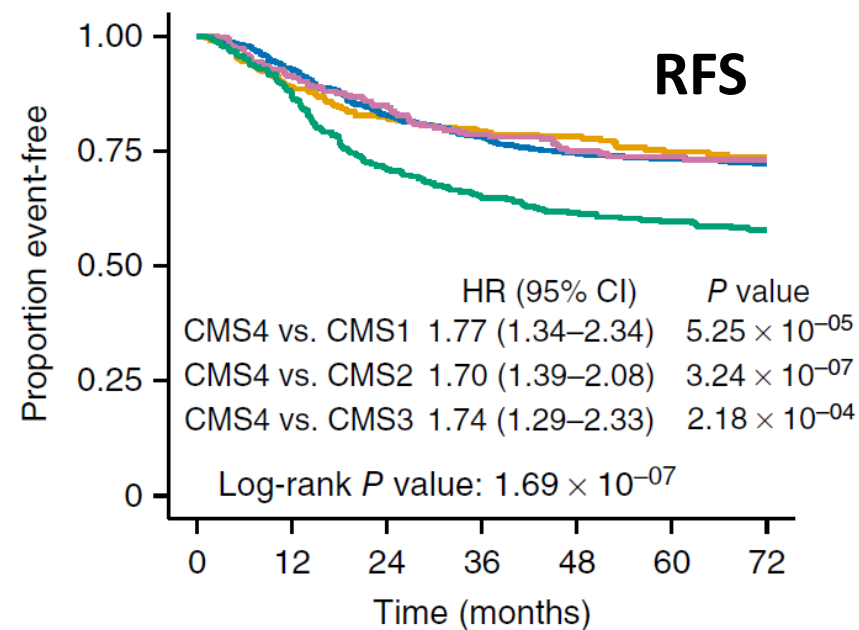
CMS2
Canonical

CMS3
Metabolic

CMS4
Mesenchymal

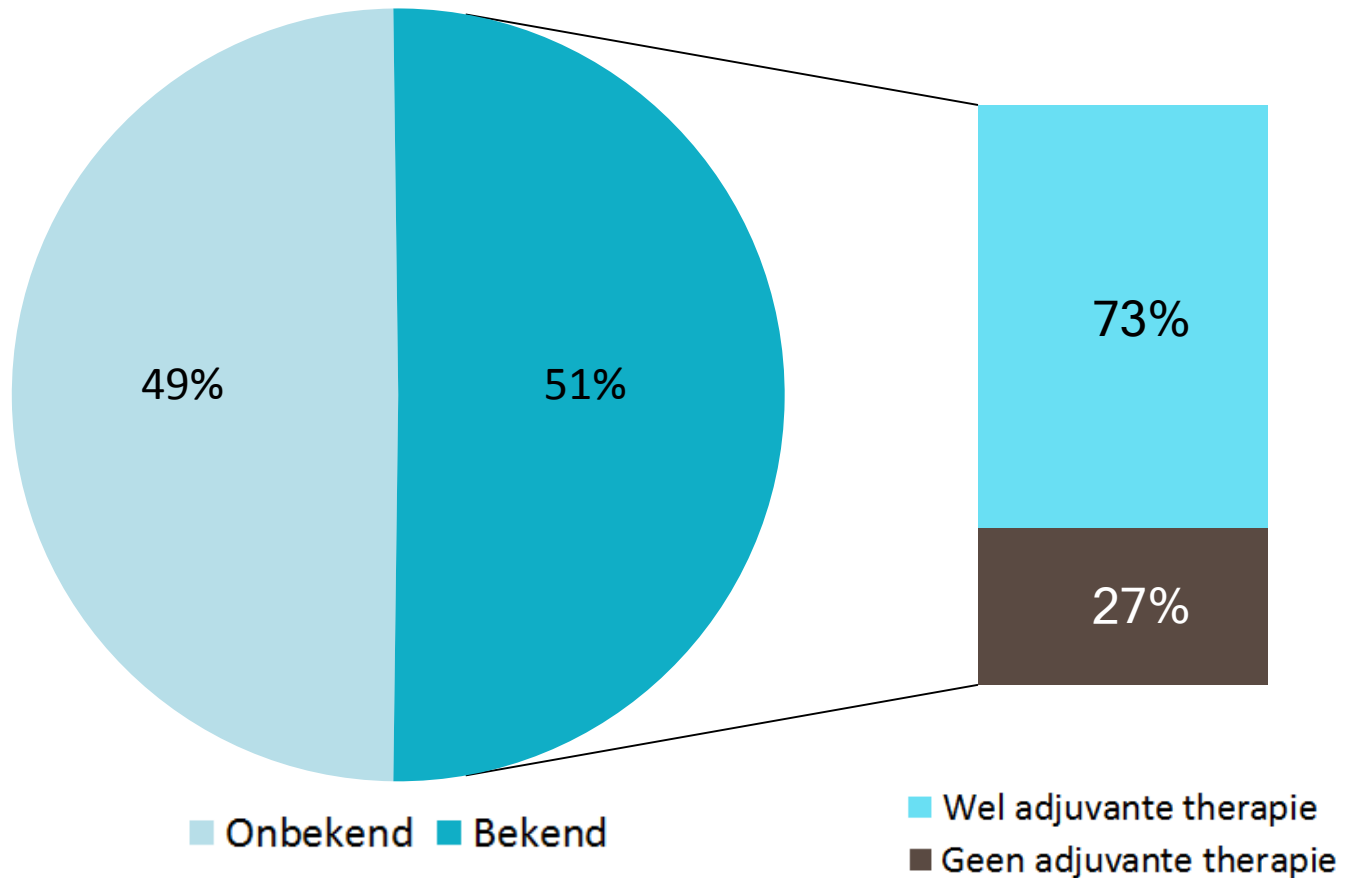


Number at risk 2,129 1,842 1,623 1,442 1,237 1,009 767

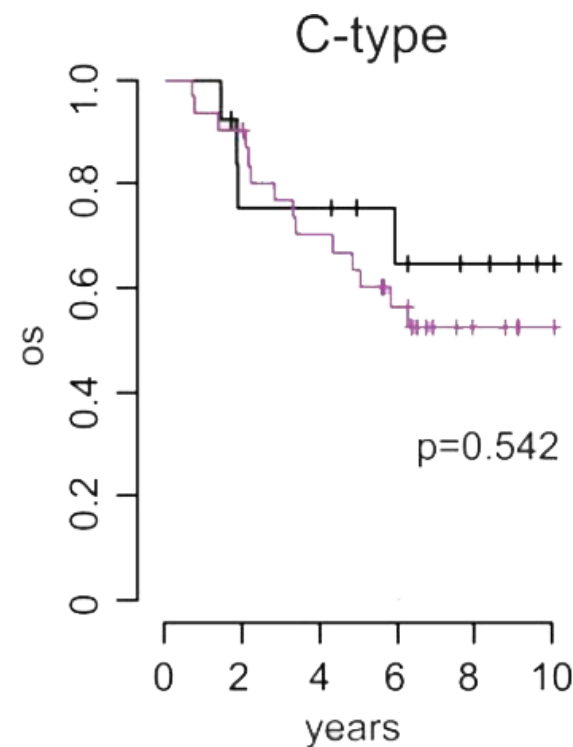
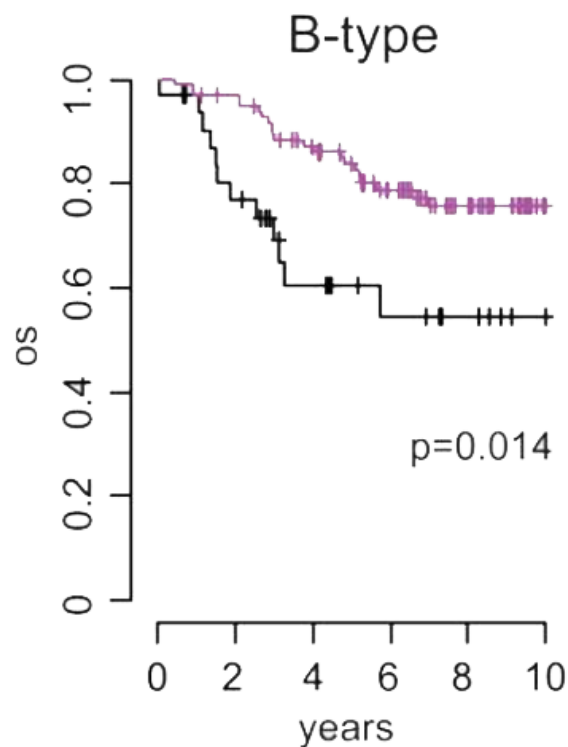
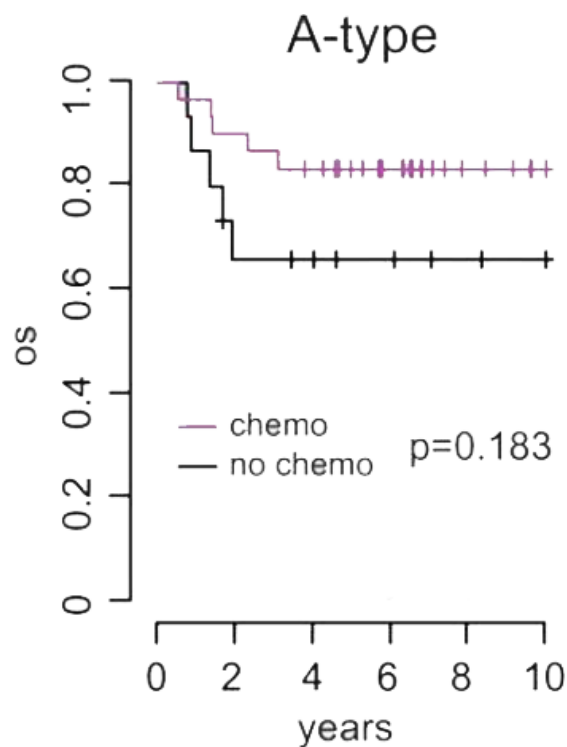


1,785 1,571 1,332 1,168 992 820 693

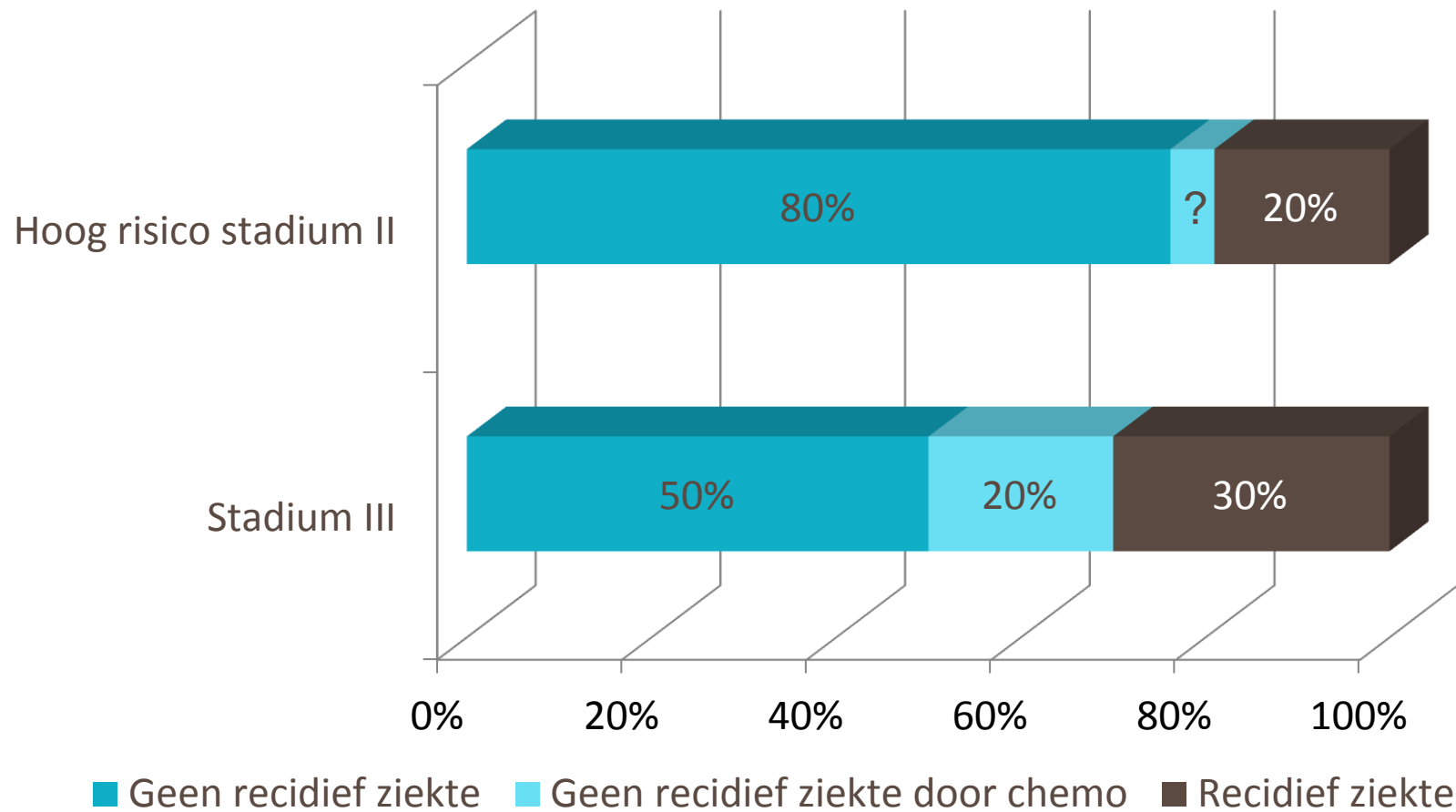
Driekwart van de patiënten kreeg adjuvante therapie



A- en B-type lijken baat te hebben bij chemo, C-type niet



**Is de respons op chemotherapie verschillend
per subtype?**



0-meting



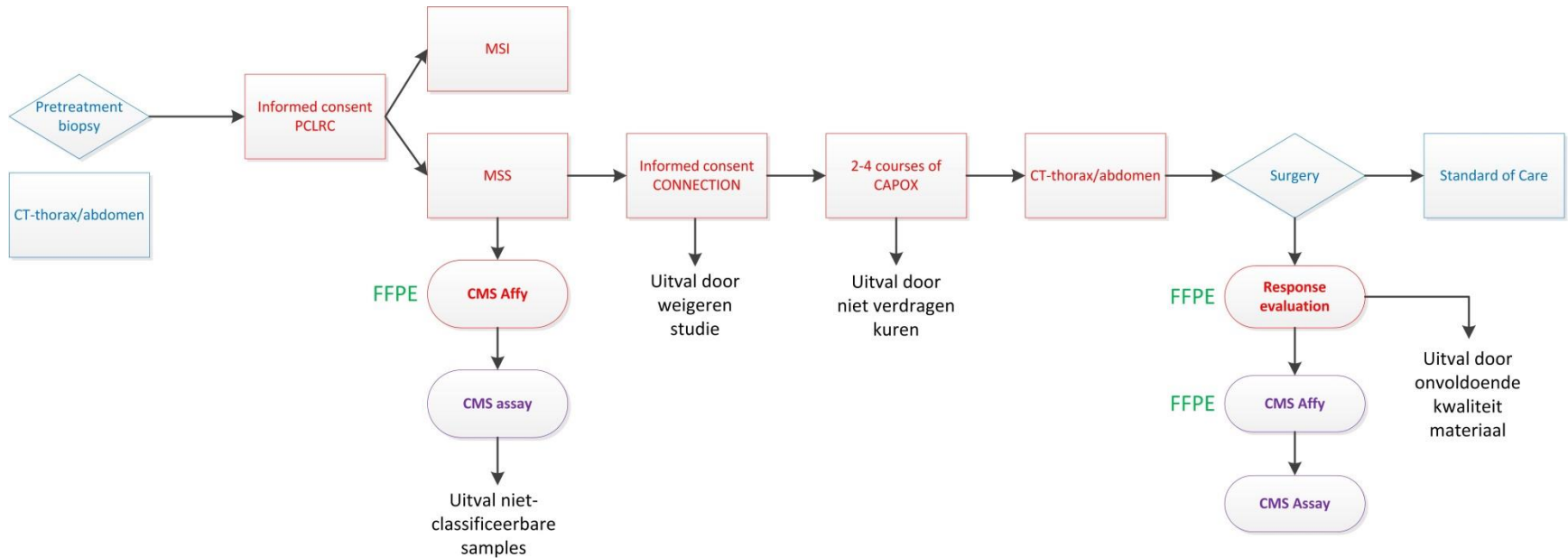
chemotherapie



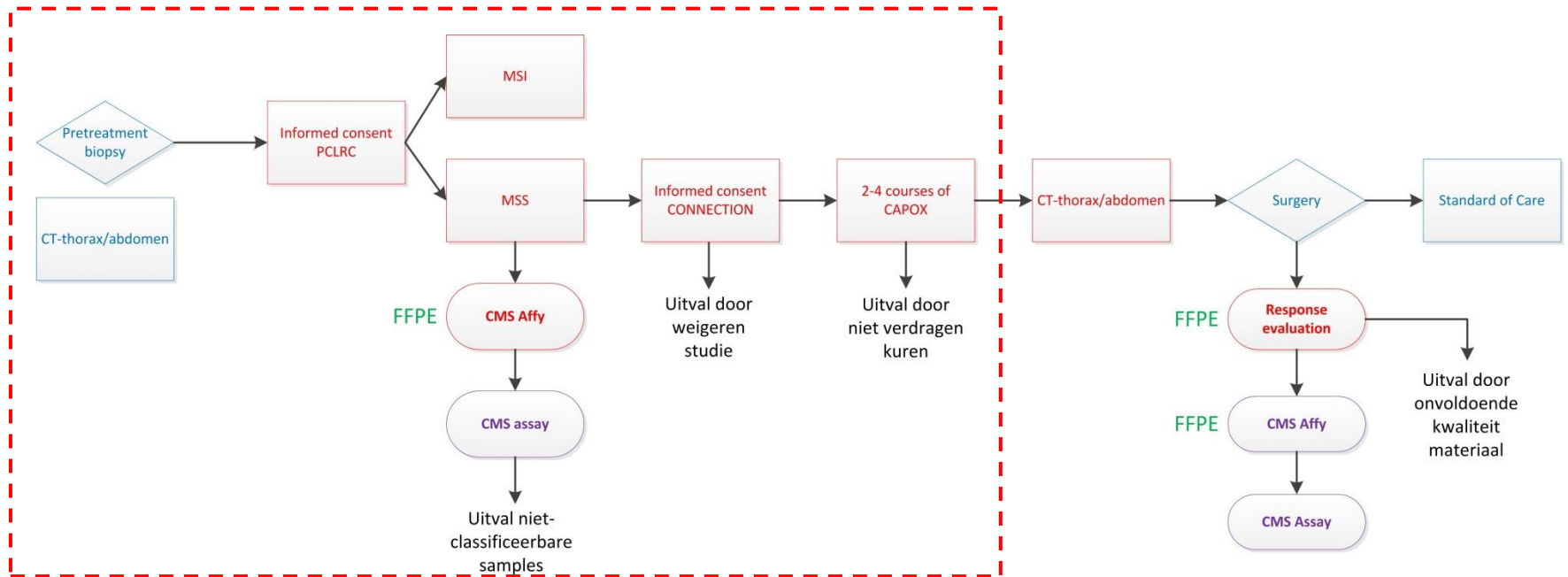
1-meting



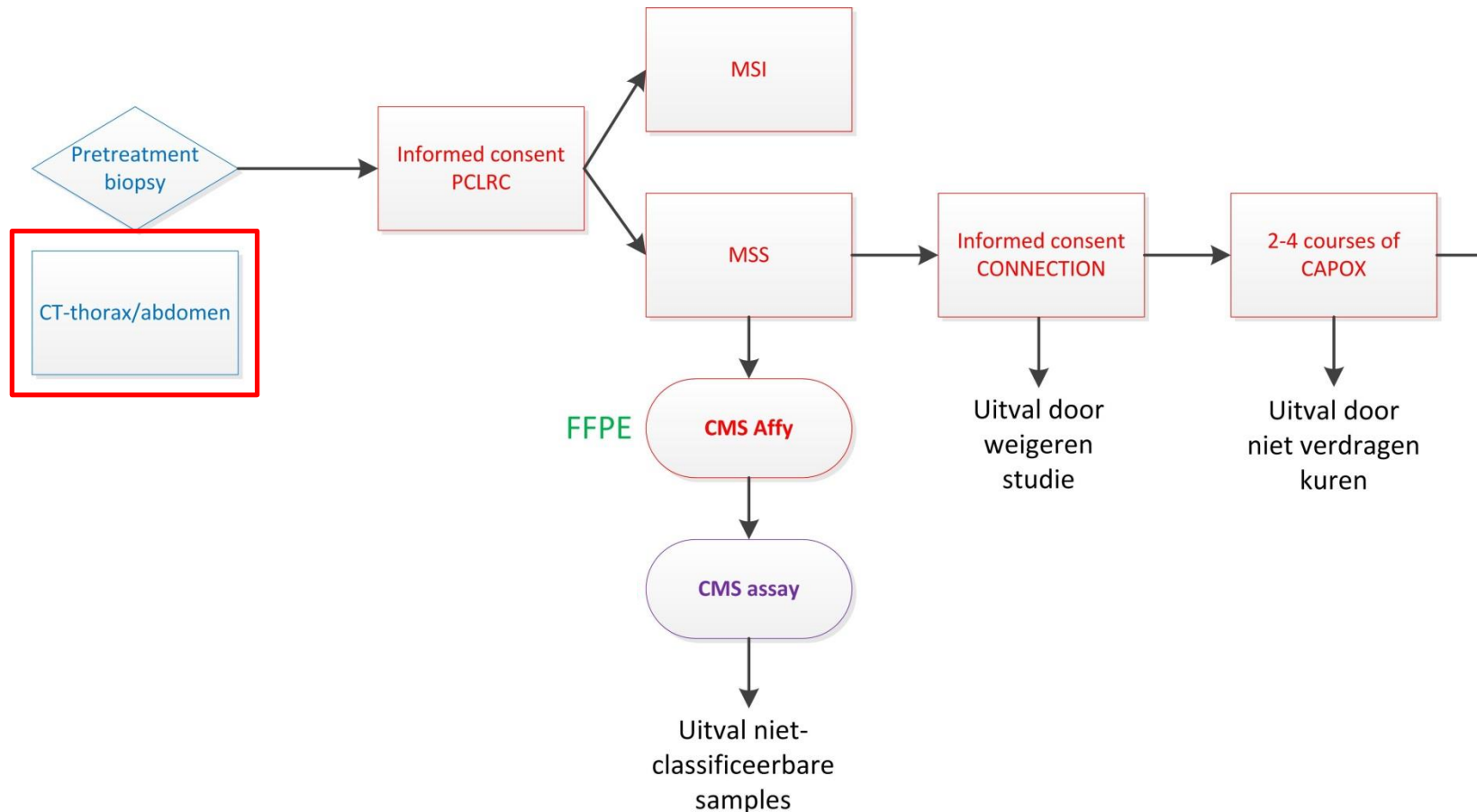
Flow chart van de studie



Flow chart van de studie



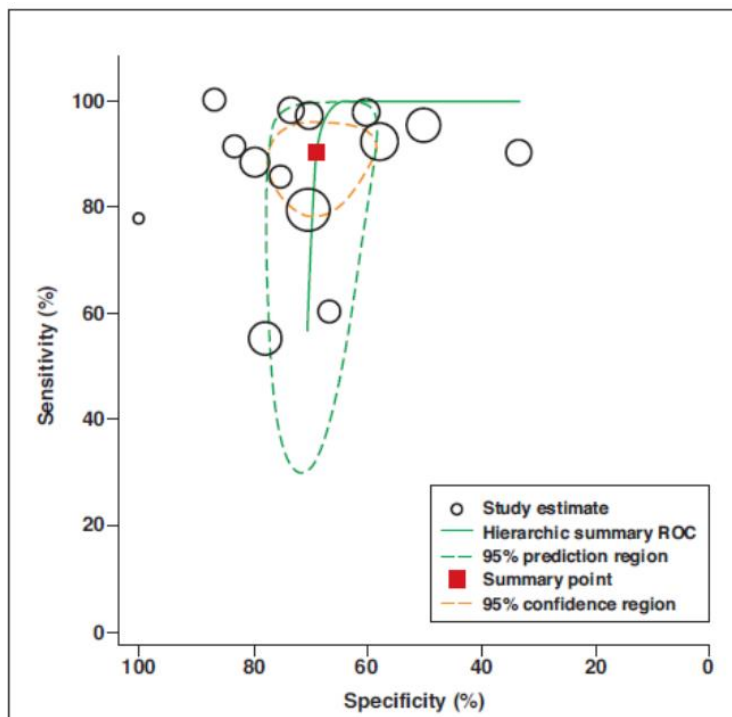
Selectie hoog risico stadium II en stadium III moet op basis van het cTNM stadium



T-stadium is betrouwbaar te bepalen, N-stadium niet

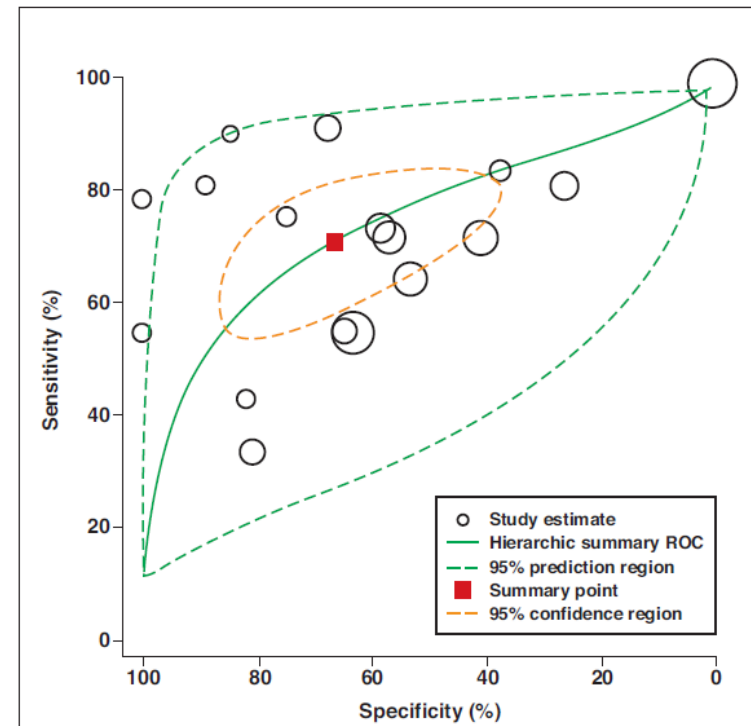
T1-2 vs T3-4

Sensitiviteit 90% (83-95%)
Specificiteit 69% (62-75%)

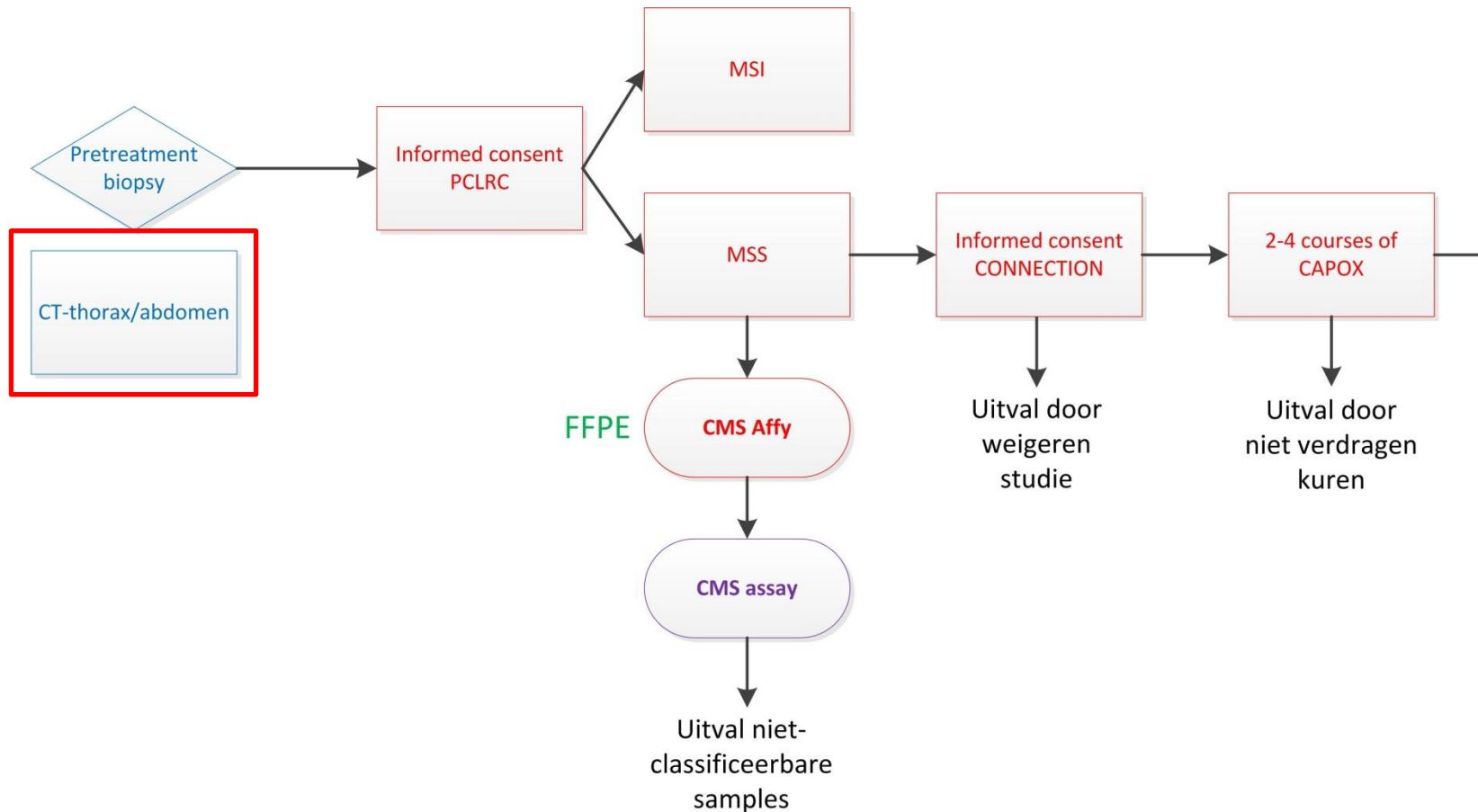


Nodal involvement

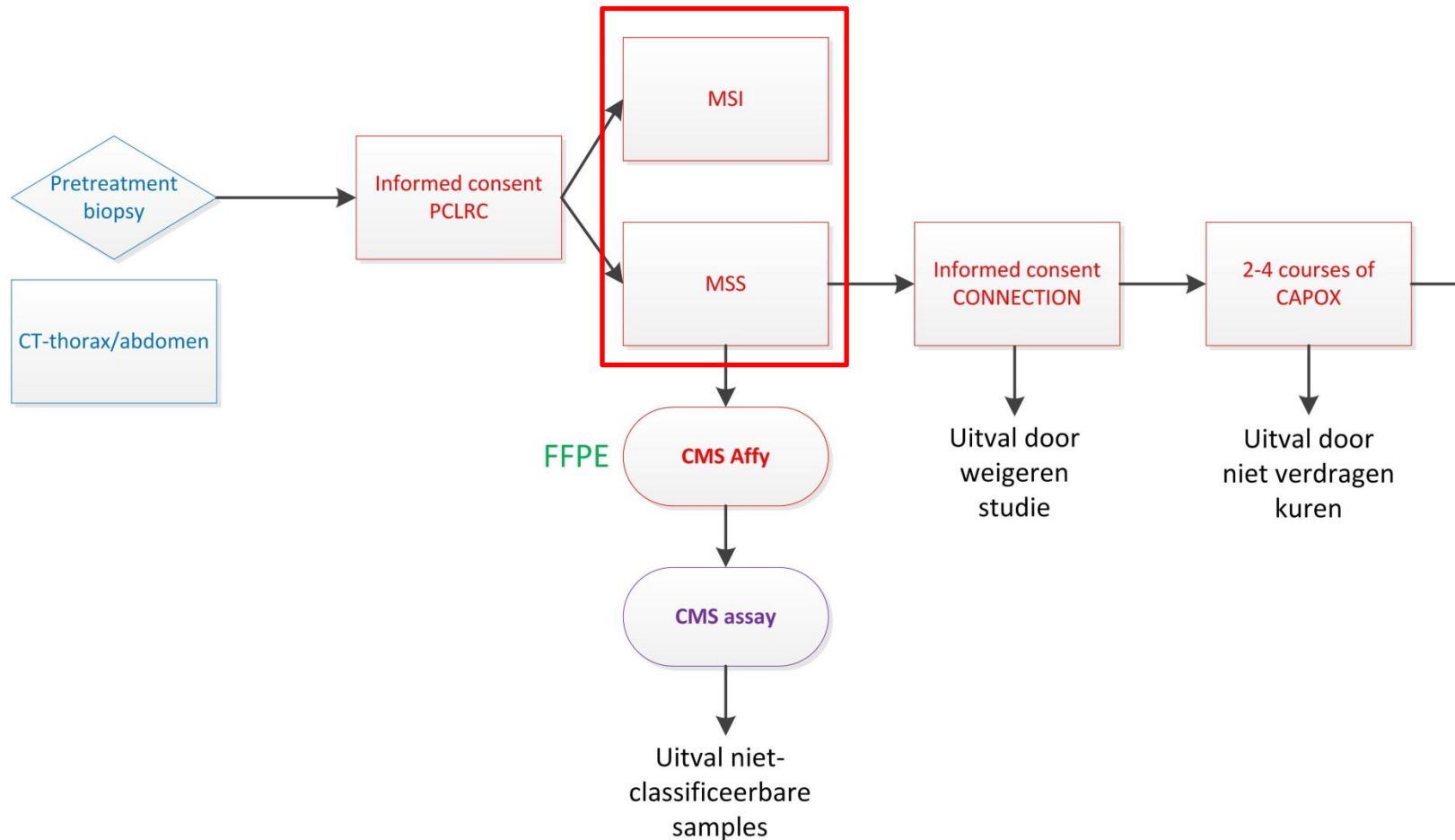
Sensitiviteit 71% (59-81%)
Specificiteit 67% (46-83%)



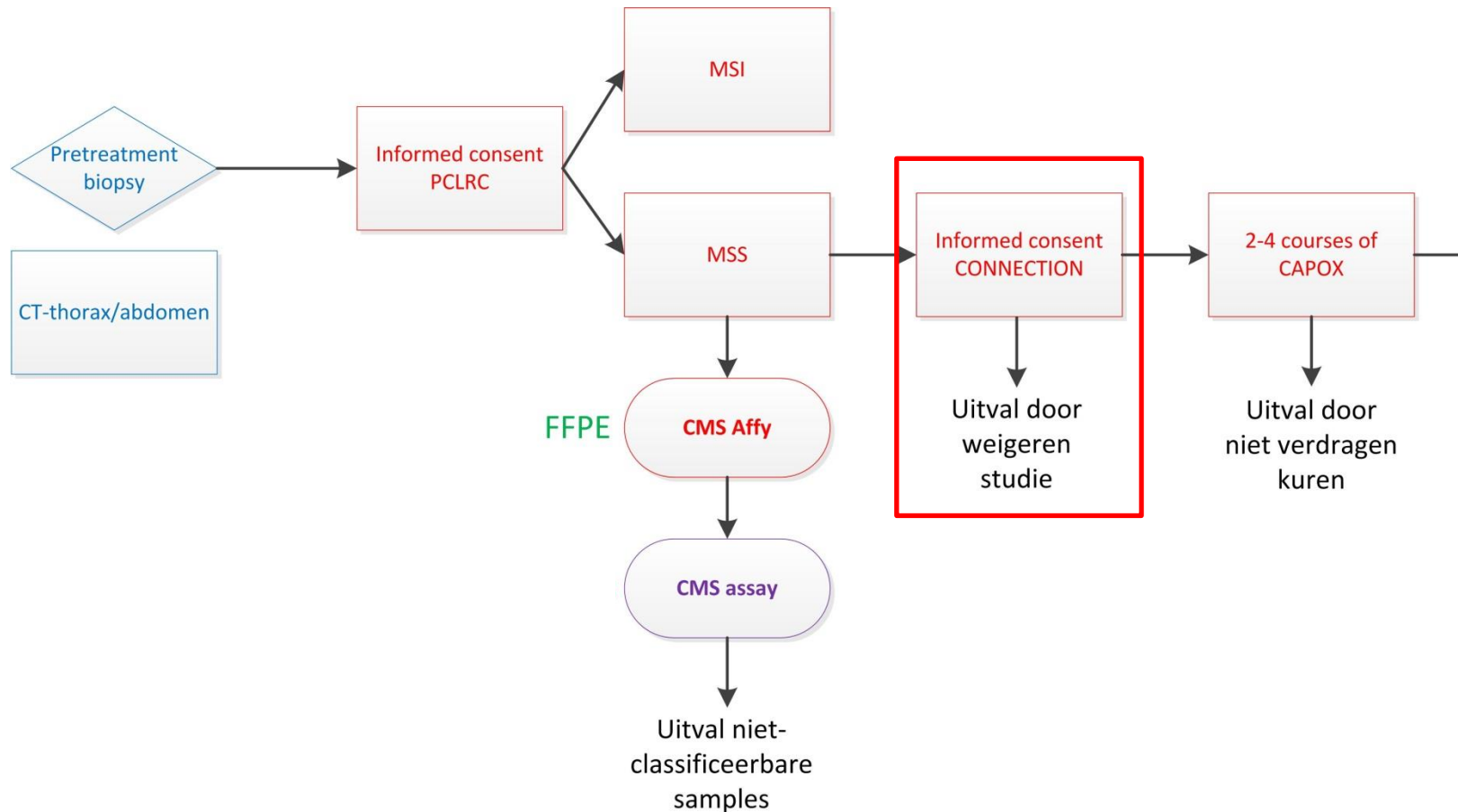
cT3-4N0-2M0 colon carcinoom



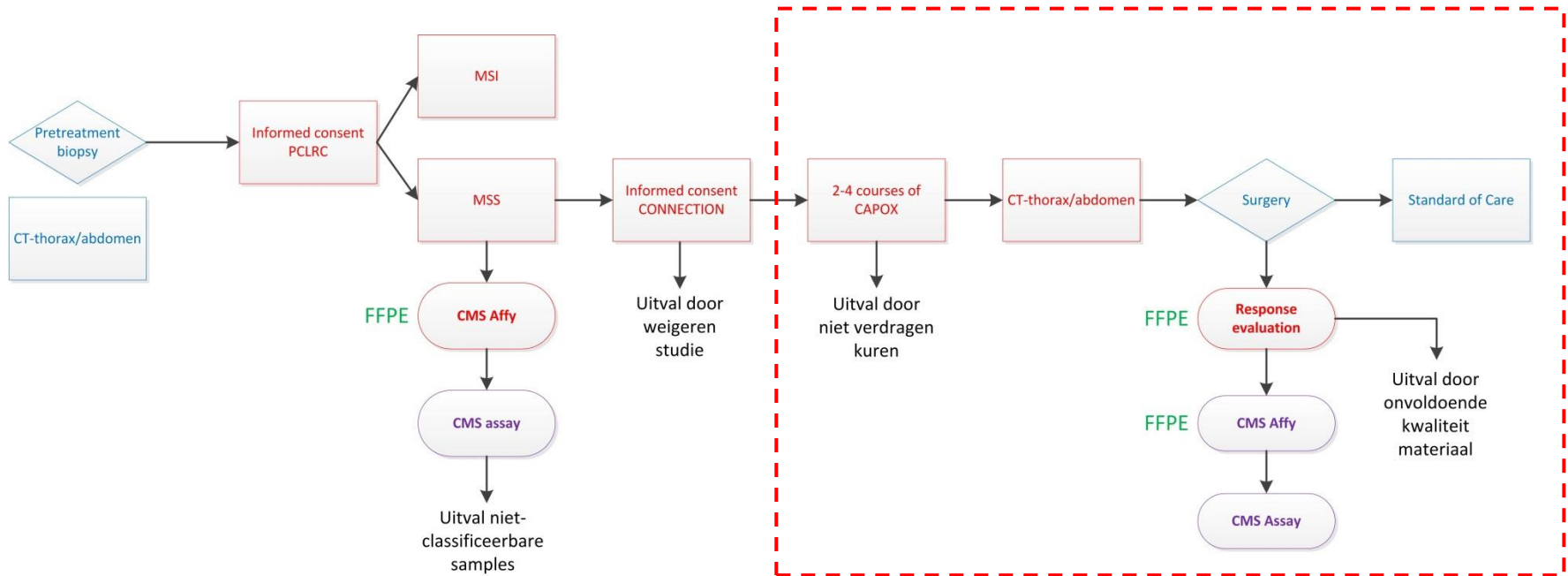
cT3-4N0-2M0 MSS colon carcinoom



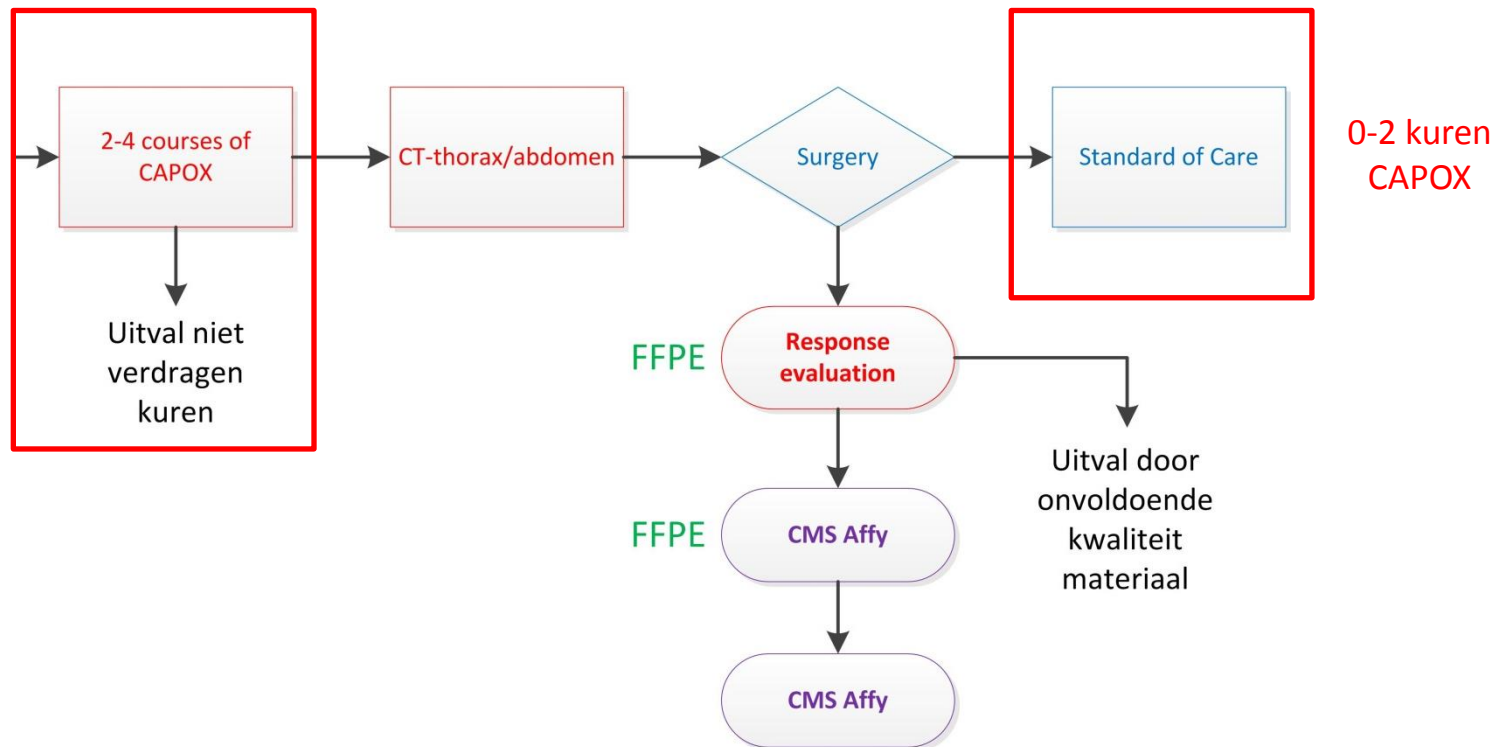
cT3-4N0-2M0 MSS colon carcinoom



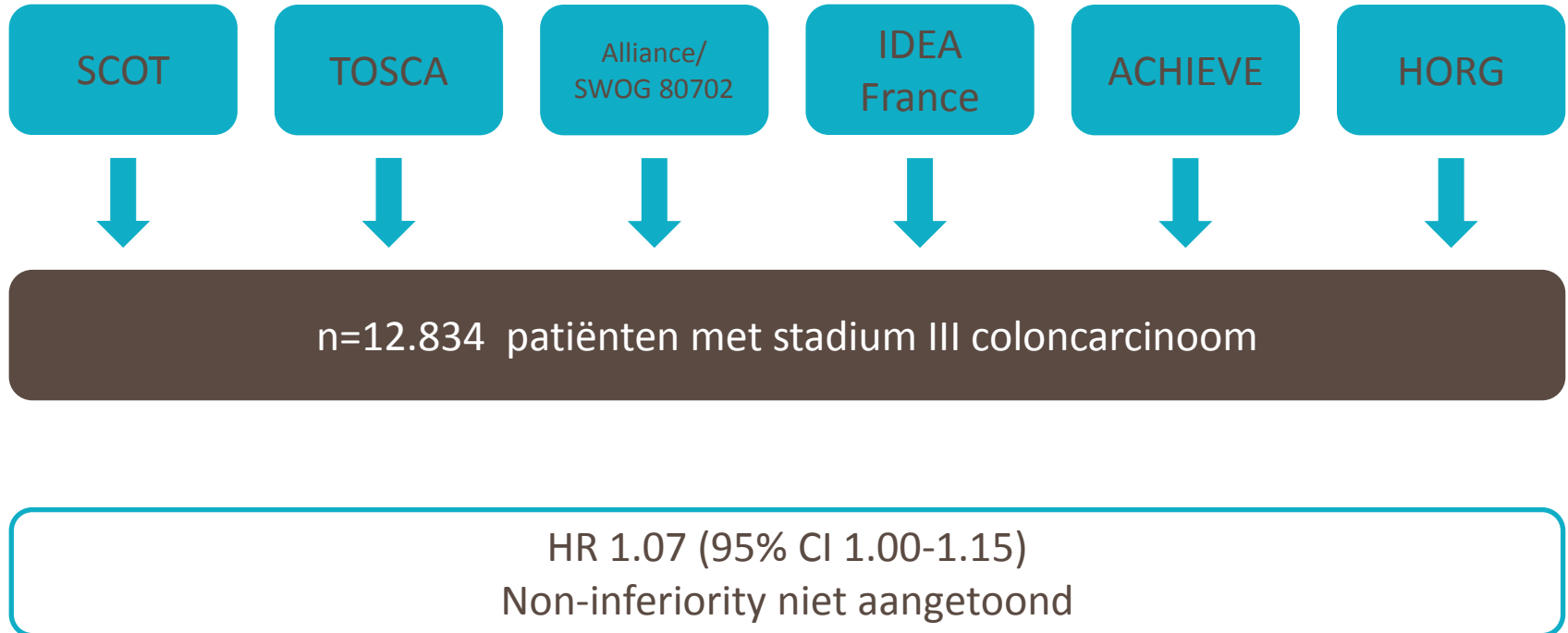
Flow chart van de studie



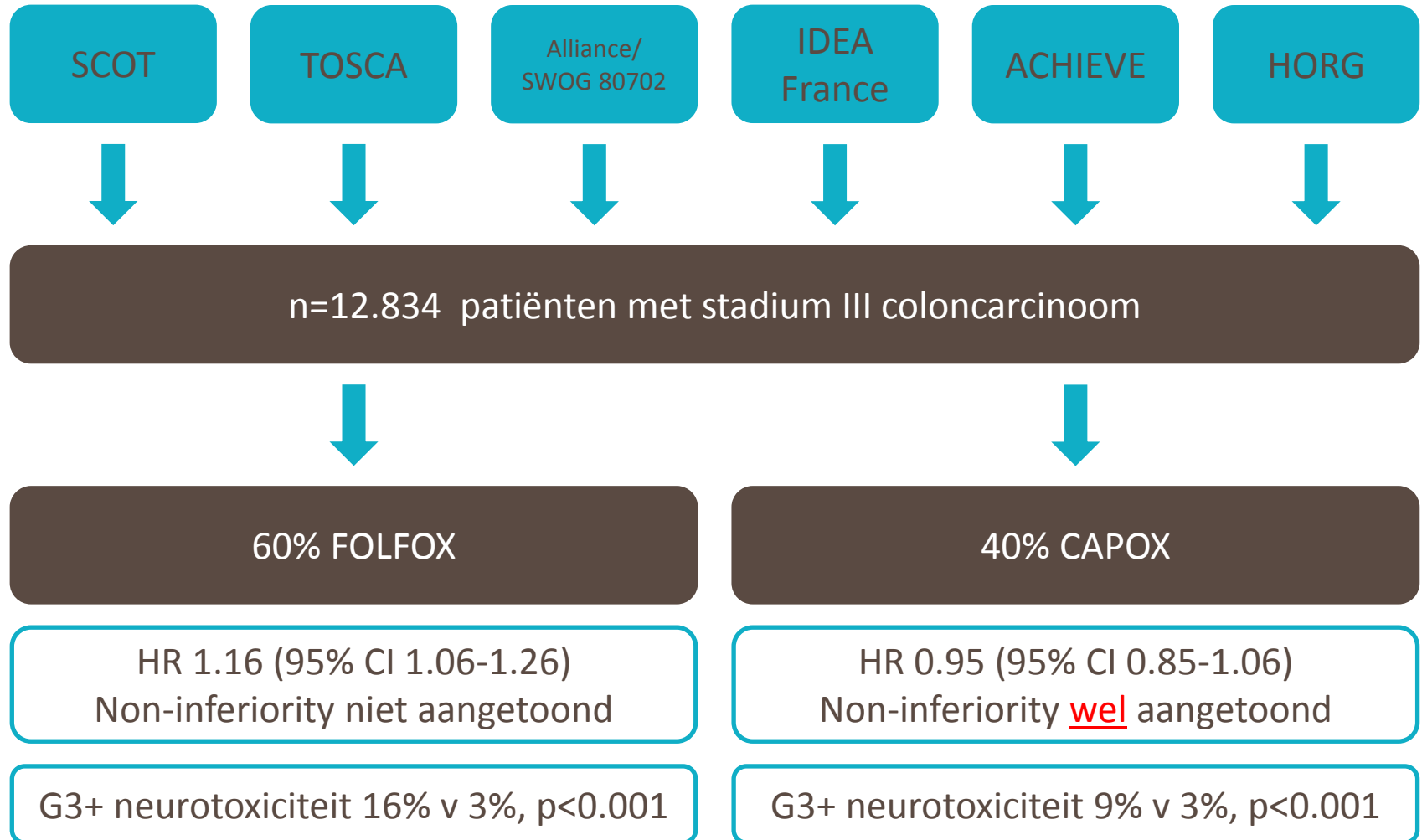
Totale behandelduur CAPOX van 6 naar 3 maanden op basis van data gepresenteerd op ASCO



Geplande gepoolde analyse 6 maanden versus 3 maanden CAPOX/FOLFOX (non-inferiority)

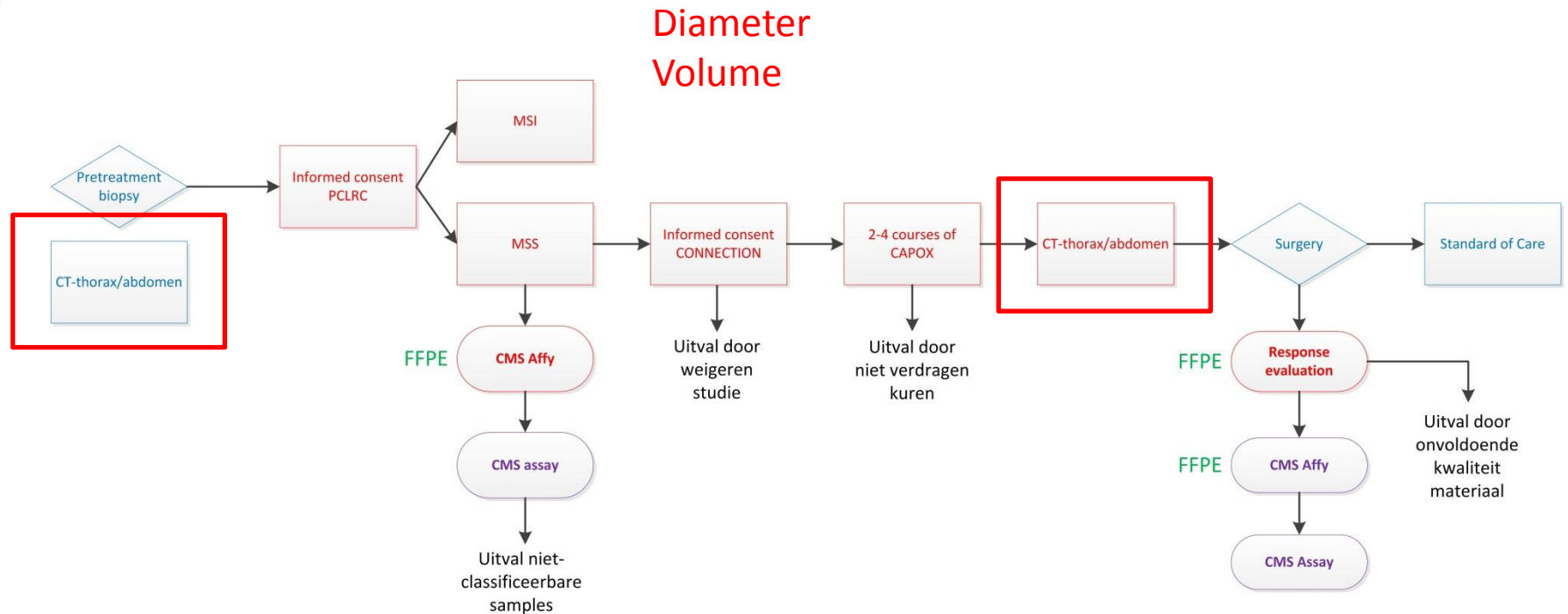


Geplande gepoolde analyse 6 maanden versus 3 maanden CAPOX/FOLFOX (non-inferiority)



Primaire eindpunt: tumor respons

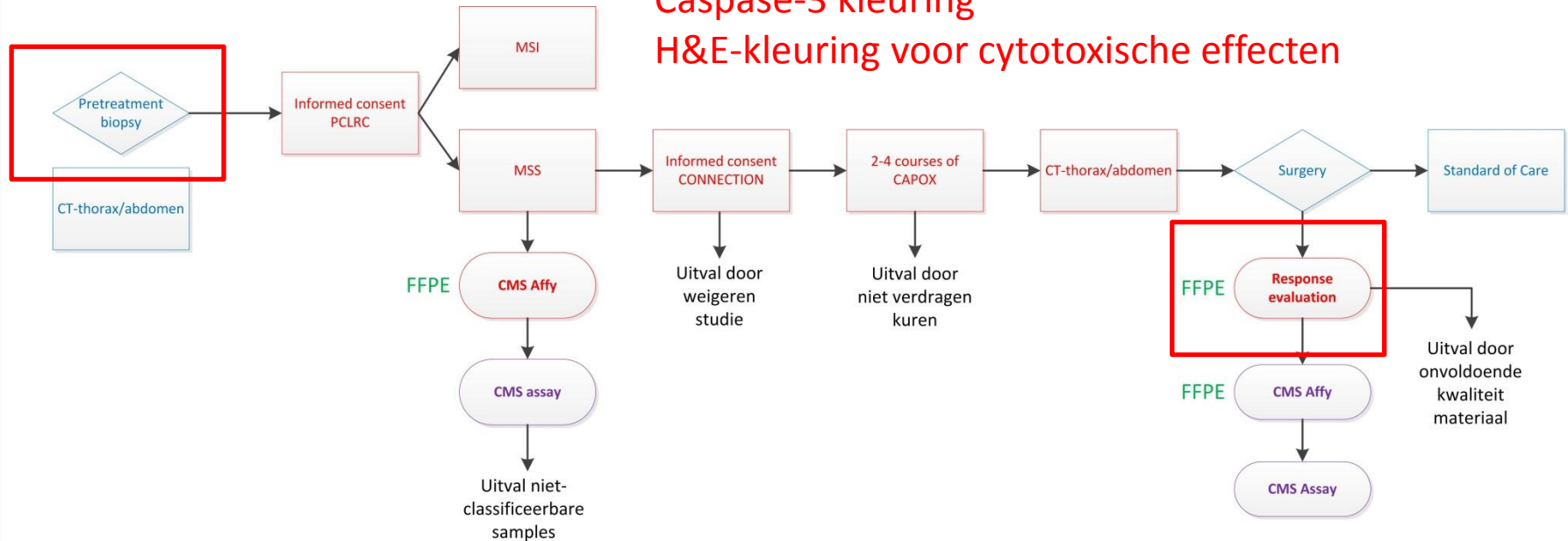
Klinisch



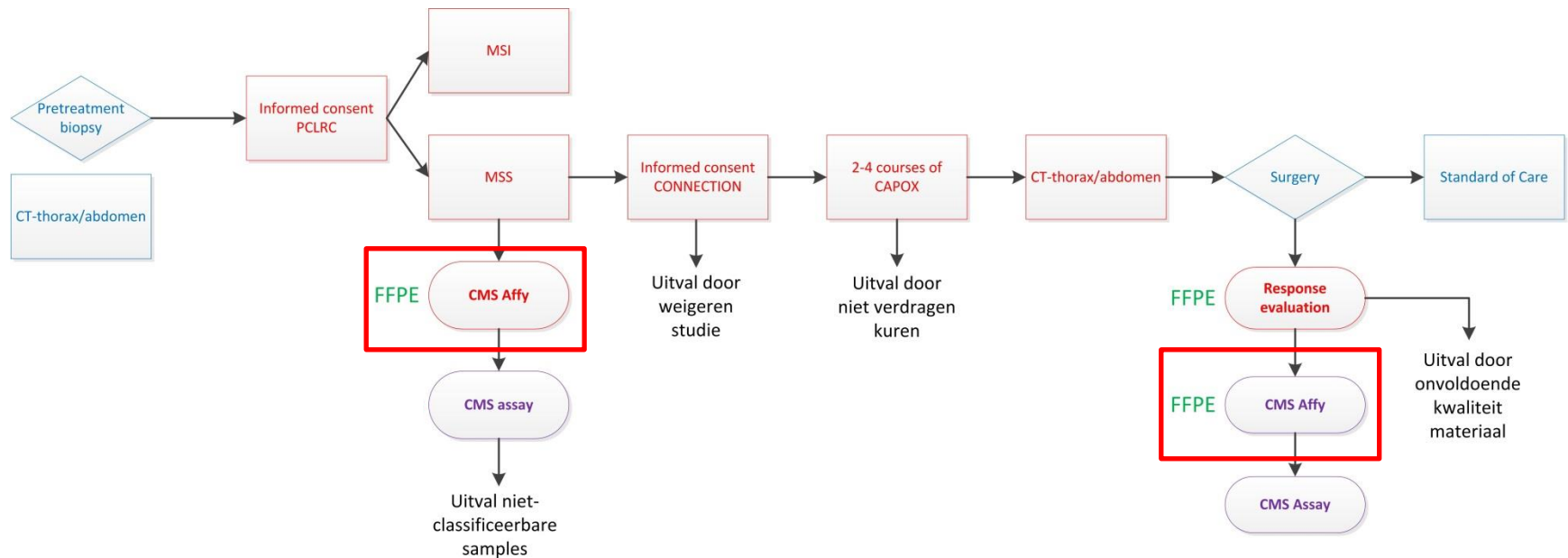
Primaire eindpunt: tumor respons

Pathologisch

Ki-67 kleuring
Caspase-3 kleuring
H&E-kleuring voor cytotoxische effecten



Secundair eindpunt: therapie geïnduceerde CMS verandering



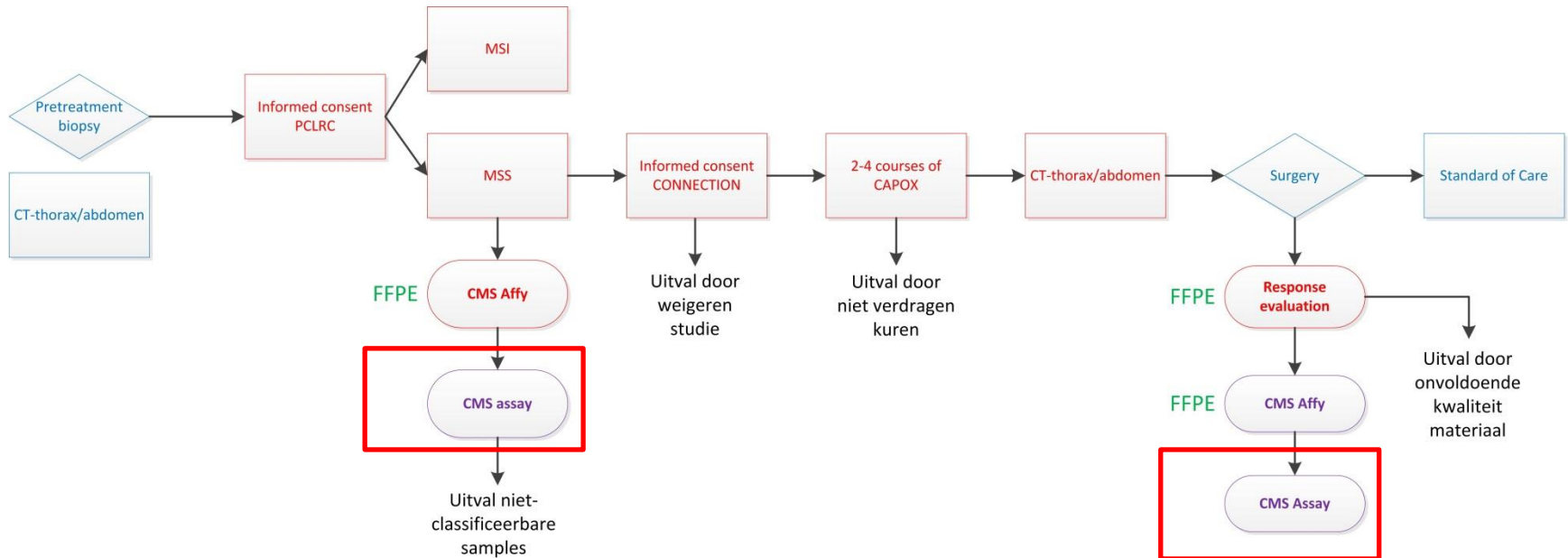
Standaard zorg

Studie

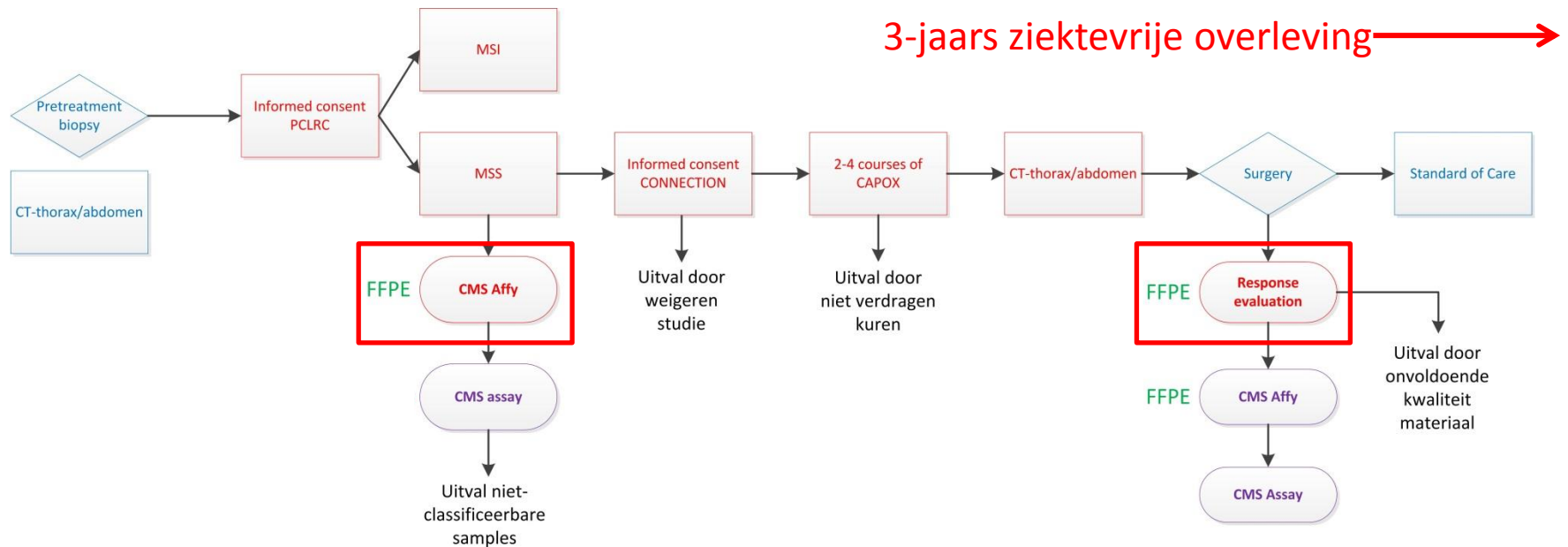
Type materiaal

Nodig voor secundair eindpunt

Secundair eindpunt: validatie van een CMS assay



Secundair eindpunt: associatie respons met 3-jaars ziektevrije overleving



Aantallen

- Primaire eindpunt 158 patiënten
- Secundaire eindpunt 539 patiënten
(3-jaars ziektevrije overleving)
- 6 ziekenhuizen

Logistieke uitdaging



Logistieke uitdaging

Haalbaarheid?



Logistieke uitdaging

Haalbaarheid?

Hoeveel kuren neoadjuvant en adjuvant?



Logistieke uitdaging

Haalbaarheid?

Hoeveel kuren neoadjuvant en adjuvant?

