Optimalisatie van de moleculaire diagnostiek in de zorgketen voor longkankerpatiënten met niet-kleincellig longcarcinoom

Léon van Kempen
Klinisch Moleculair Bioloog in de Pathologie
UZA
Dienst Pathologie
Hoofd Moleculaire Diagnostiek

Wat was het aantal nieuwe diagnoses invasieve longkanker in 2021?

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Active poll

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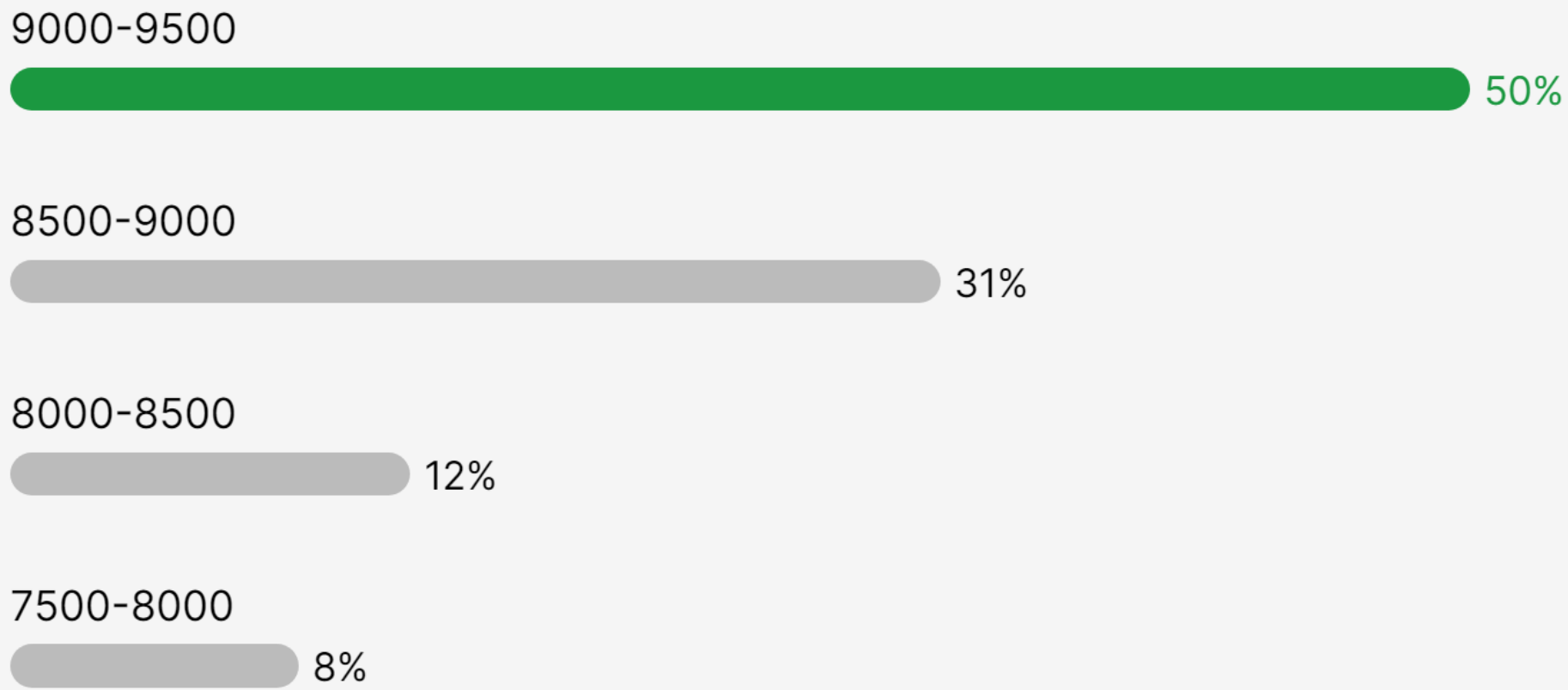
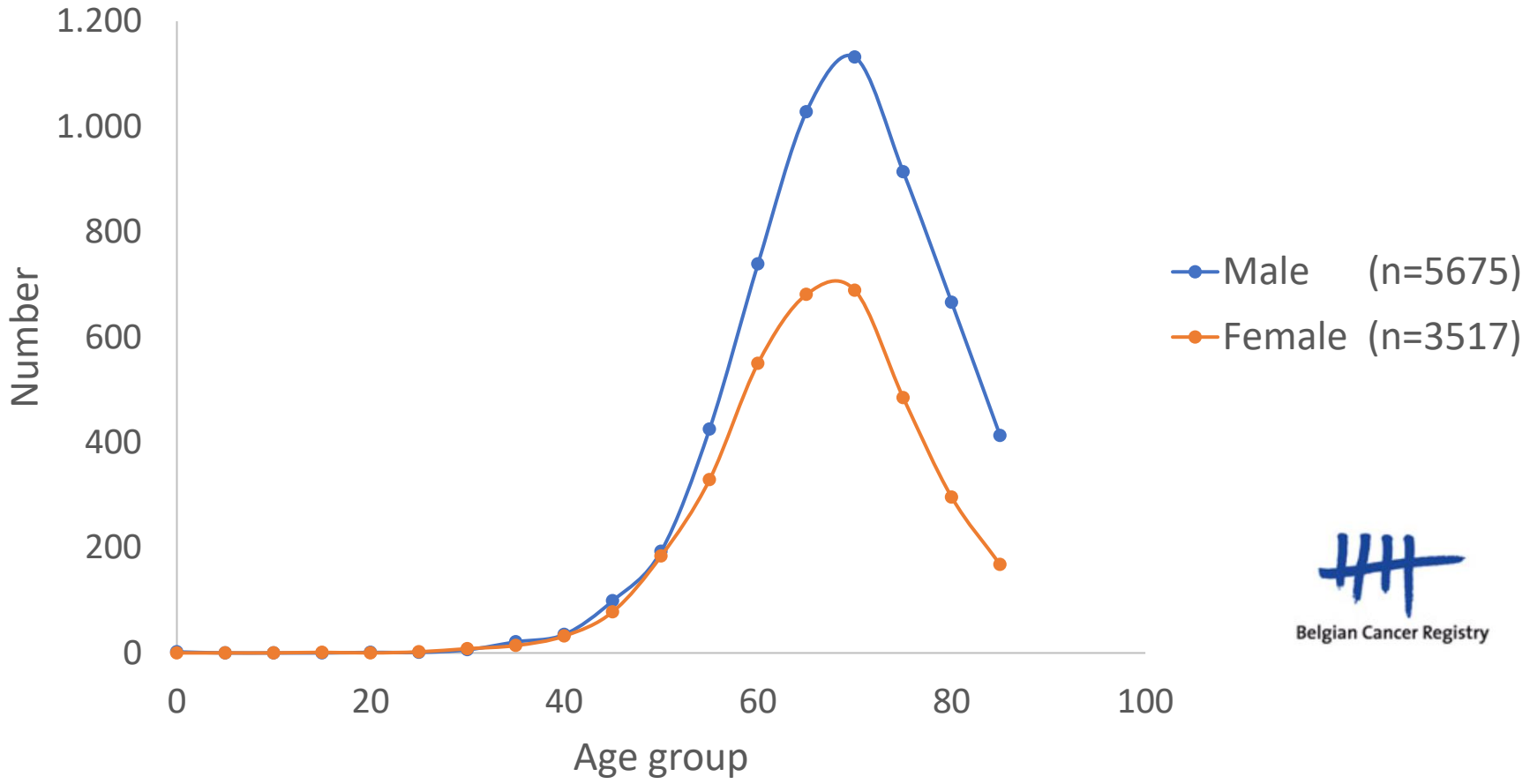
Wat was het aantal nieuwe diagnoses invasieve longkanker in 2021?



Aantal nieuwe diagnoses invasieve longkanker in België 2021: N=9192



Longkanker in België 2018

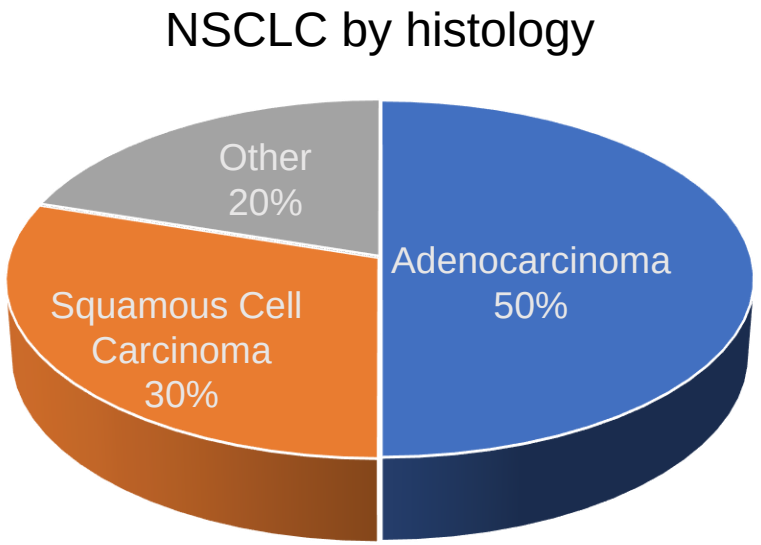
Table 1. Stage Distribution of Lung Cancer by Sex and Histologic Type in Belgium in 2018[9]

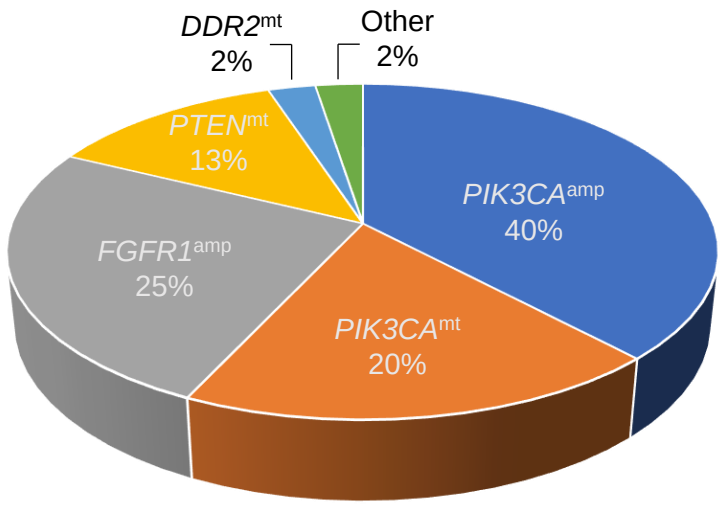
	Males		Females	
	NSCLC	SCLC	NSCLC	SCLC
Stages	n (%)	n (%)	n (%)	n (%)
I	811 (18)	59 (8)	554 (24)	29 (6)
II	367 (8)		170 (7)	
III	978 (22)	166 (21)	424 (18)	127 (27)
IV	2009 (46)	495 (63)	1091 (47)	288 (61)
Unknown	219 (5)	62 (8)	101 (4)	26 (6)

BCR, Belgian Cancer Registry.
Reprinted with permission from BCR.

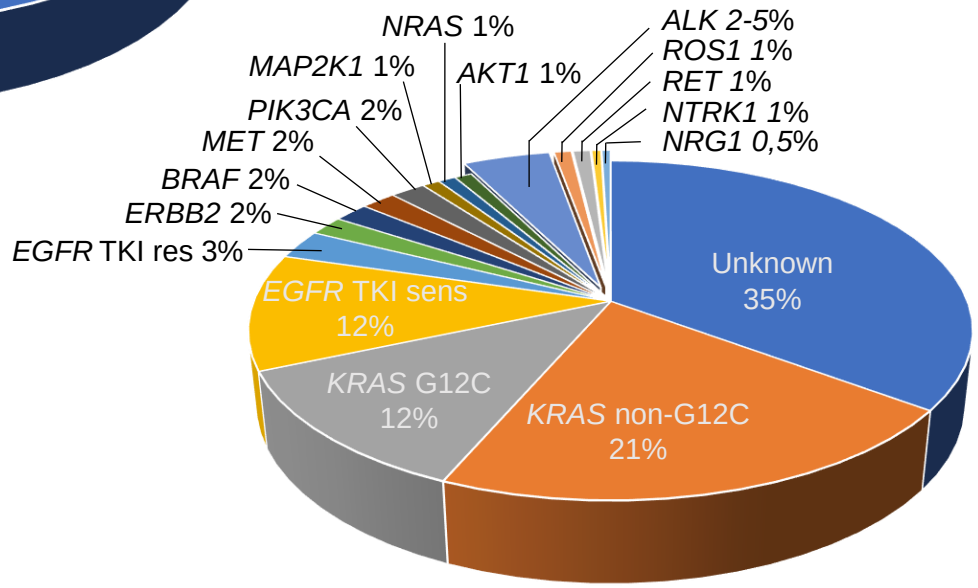
Lung cancer in Belgium. *Journal of Thoracic Oncology* 2021, 16(10):1610-1621

Moleculaire drivers in adeno en squameus NSCLC





Squamous Cell Carcinoma



Adenocarcinoma

Koopman et al. 2021; Garcia et al 2022; Steeghs et al 2022; De Jager et al under review

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Welke van deze genen moeten naast EGFR, ALK en KRAS getest worden bij de primaire diagnose van stadium IV nsqNSCLC?

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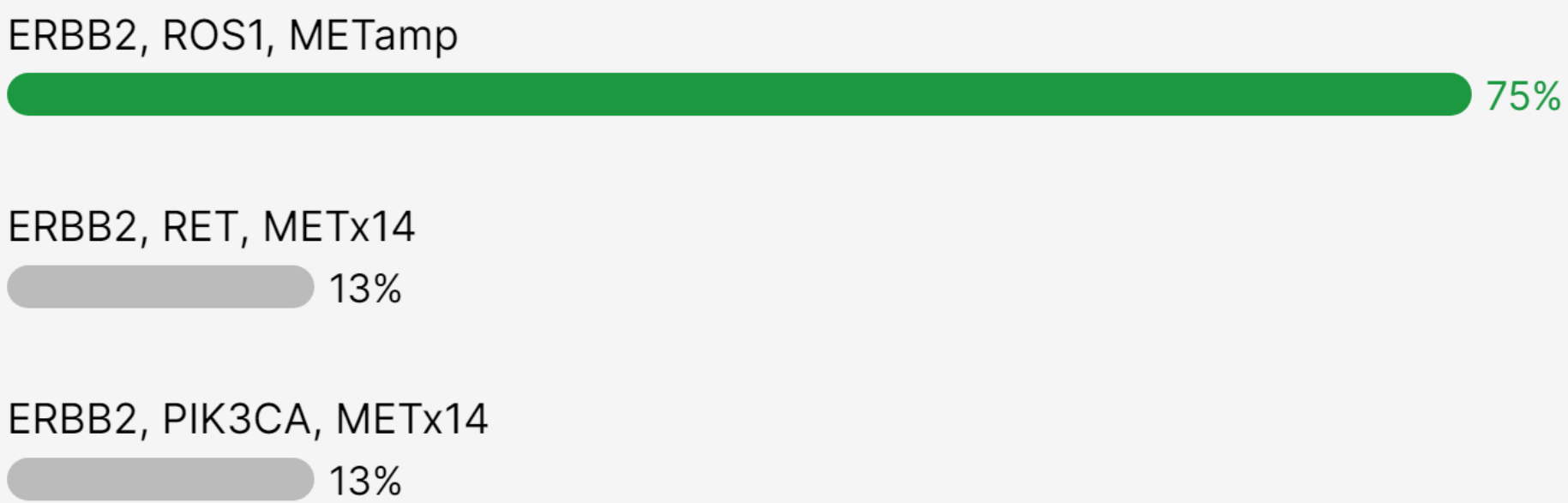
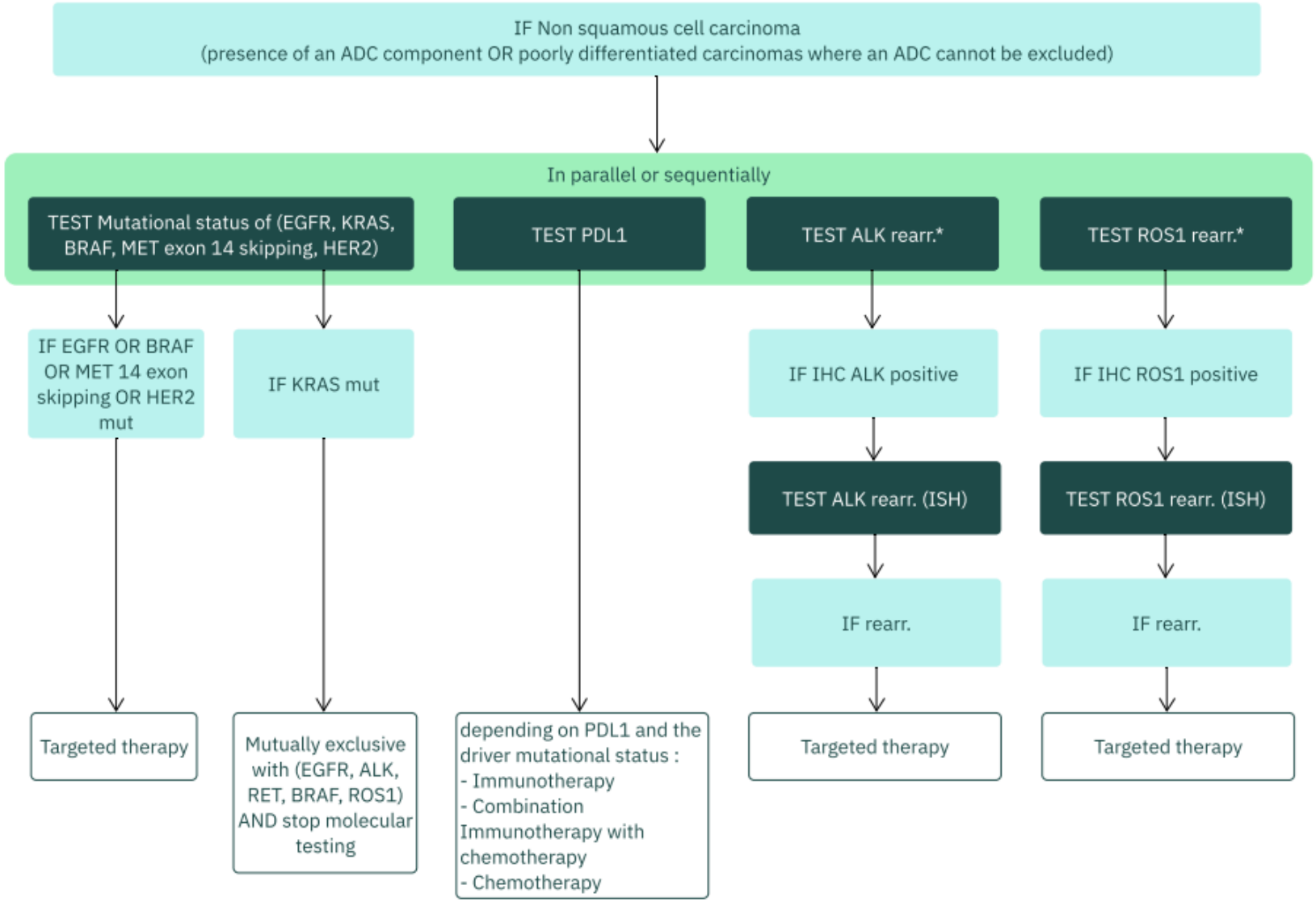
Welke van deze genen moeten naast EGFR, ALK en KRAS getest worden bij de primaire diagnose van stadium IV n-sq NSCLC?



www.compermed.be : test algoritme nsqNSCLC

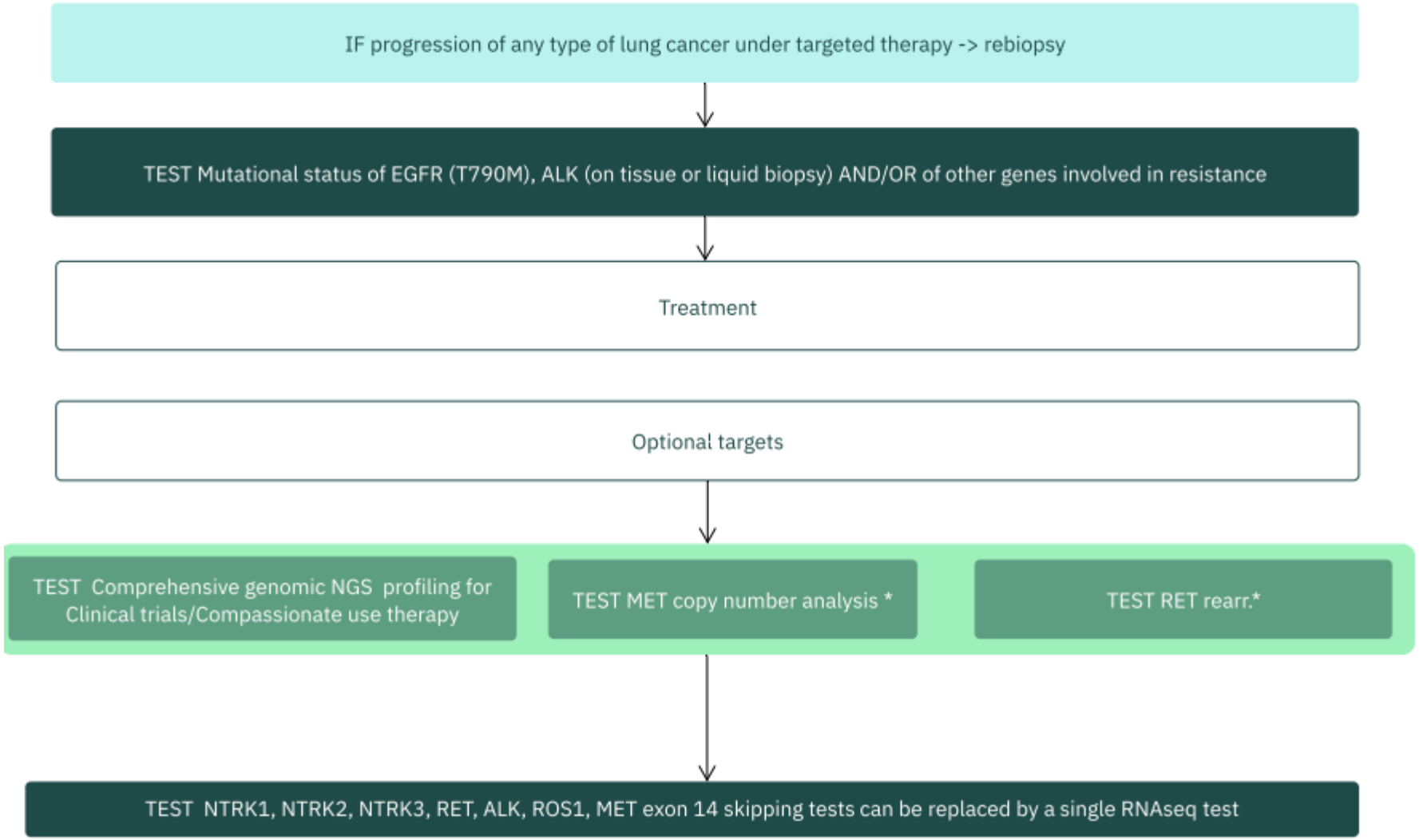


Test level 1 & 2A : Molecular tests are recommended

Test level 2B : Molecular tests are not yet recommened

These workflows are considered as a tool for good clinical practice. Some of the recommended molecular tests present in the workflows are not yet reimbursed by the INAMI/RIZIV.

www.compermed.be : test algoritme nsqNSCLC



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Predictieve biomerkers NSCLC bij primaire diagnose

Alle tumoren

IHC:

PDL1

Niet-squameus en squameus nooit-roker

NGS (DNA)

EGFR

KRAS

BRAF

METx14

ERBB2

NGS (RNA)

ALK

ROS1

RET

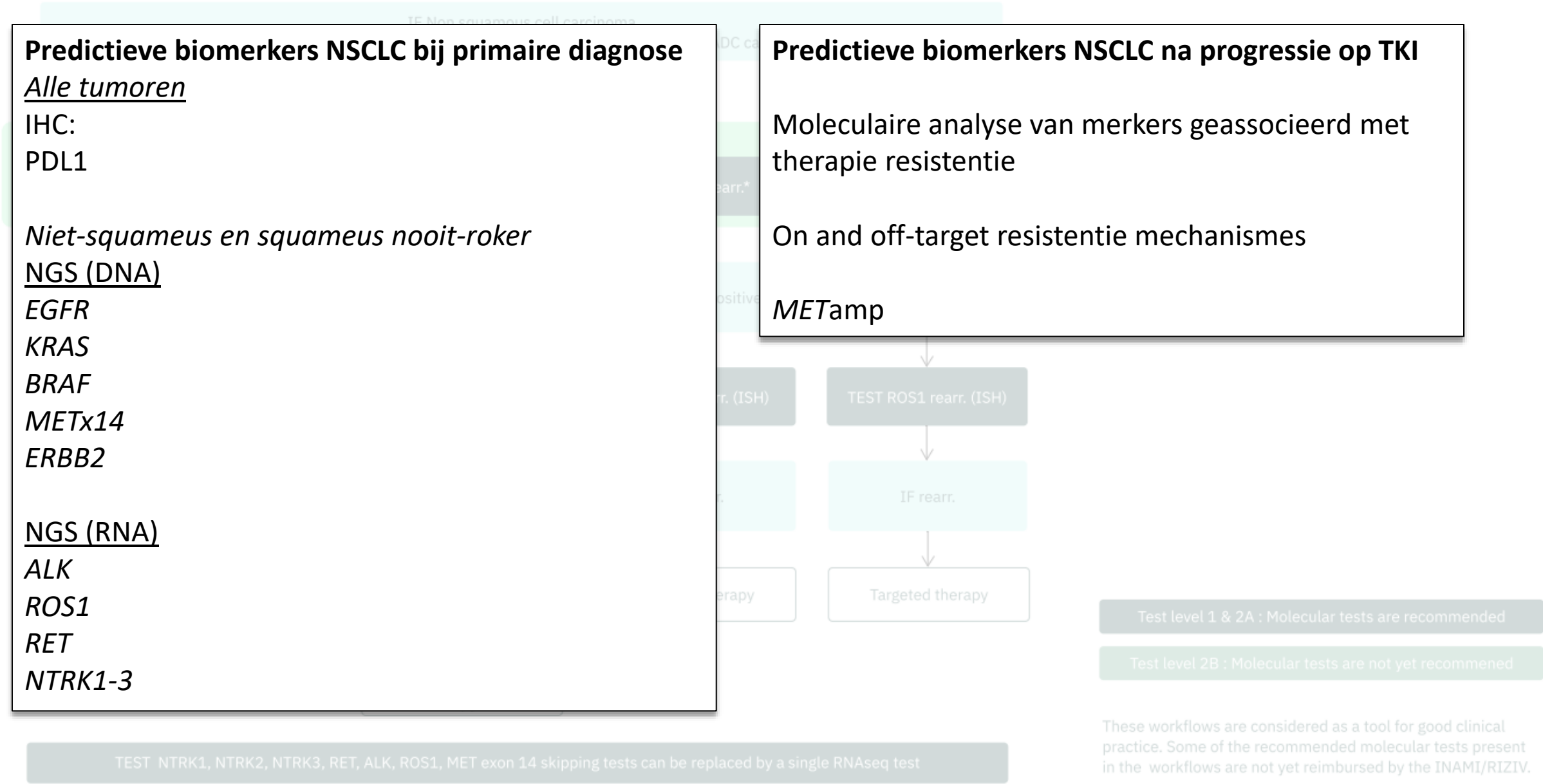
NTRK1-3

Predictieve biomerkers NSCLC na progressie op TKI

Moleculaire analyse van merkers geassocieerd met therapie resistentie

On and off-target resistentie mechanismes

*MET*amp



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*MET*amp

RIZIV

Comprehensive genomic profiling: niet vergoed

NGS ccfDNA analyse op vochten: niet vergoed

*MET*amp na NGS: niet vergoed

Wat was het percentage stadium 4 nsqNSCLC dat getest werd voor EGFR mutaties in 2019?

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Active poll

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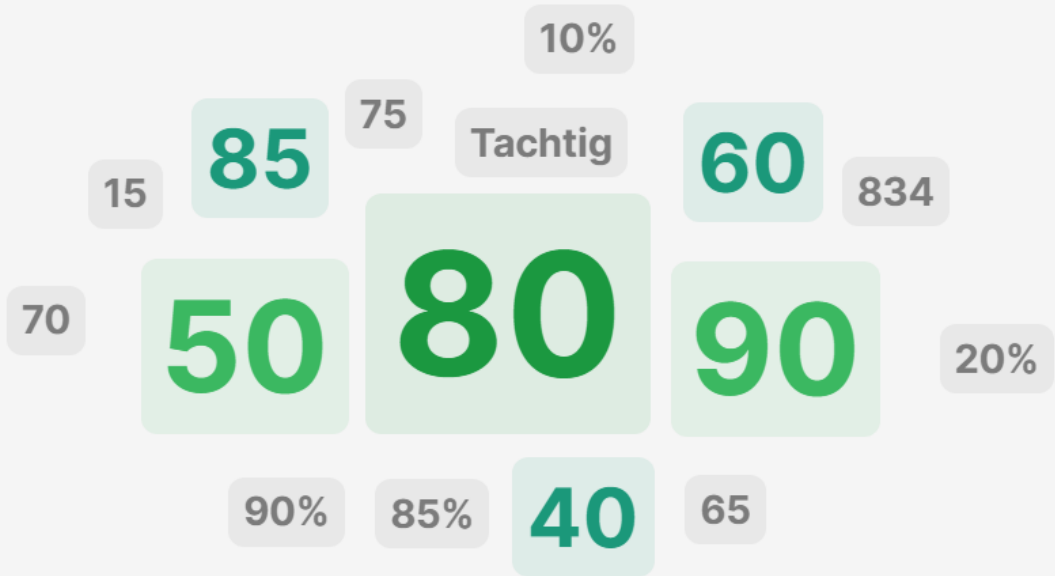
#2391 618

Wat was het percentage stadium 4 nsNSCLC dat getest werd voor EGFR mutaties in 2019?



Geen data over frequentie van *EGFR* mutatie analyse na 2011

Category and QPI Description	N	Result at National Level	Variability Between Centers
EGFR testing			
Proportion of patients with cIV nonsquamous NSCLC for whom EGFR mutation analysis was performed in 2011	1535	52.7%	Moderate, with some low outliers

Lung cancer in Belgium. *Journal of Thoracic Oncology* 2021, 16(10):1610-1621

Stadium IV NSCLC in Nederland, 2019

Table 1. Characteristics of patients diagnosed with stage IV NSCLC in the Netherlands in 2019	
Age at diagnosis, in years	67.6 (10.2)
Sex	
Male	2042 (52.7)
Female	1835 (47.3)
Type of hospital	
Non-academic	3541 (91.3)
Academic	336 (8.7)
Diagnosis	
Adenocarcinoma	3424 (88.3)
NSCLC-NOS	430 (11.1)
Adenosquamous carcinoma	23 (0.6)
Clinical staging of metastatic disease*	
cM1a	948 (24.5)
cM1b	611 (15.8)
cM1c	2312 (59.7)

Continuous data are displayed as mean (SD), categorical data are displayed as n (%).*Data not available for six patients.

De Jager et al 2023. Submitted

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integraal kankercentrum Nederland

Moleculaire analyse van stadium IV niet-squameus NSCLC in Nederland, 2019

Table 2. National predictive biomarker testing rates for patients diagnosed with stage IV NSCLC in the Netherlands in 2019 (n=3,821)

Mutation testing	
Biomarker	**Overall testing rate**
EGFR	86.0% (n=3,334)
KRAS	89.0% (n=3,451)
BRAF	84.7% (n=3,283)
ERBB2	80.3% (n=3,114)
MET	73.9% (n=2,864)
Fusion testing	
Biomarker	**Overall testing rate**
ALK	63.9% (n=2,477)
ROS1	56.8% (n=2,201)
RET	31.8% (n=1,231)
NTRK	12.6% (n=489)

De Jager et al 2023. Submitted

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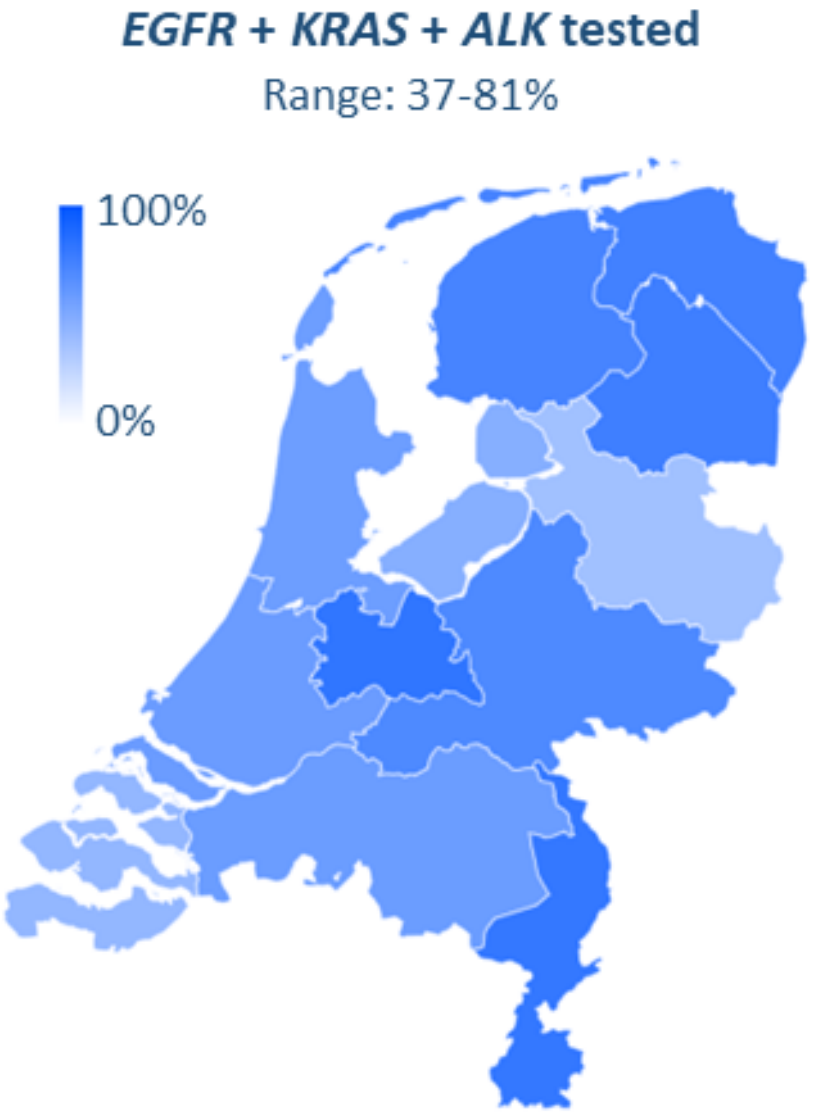
Regionale verschillen in test frequentie in 2019



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KNL integraal kankercentrum Nederland

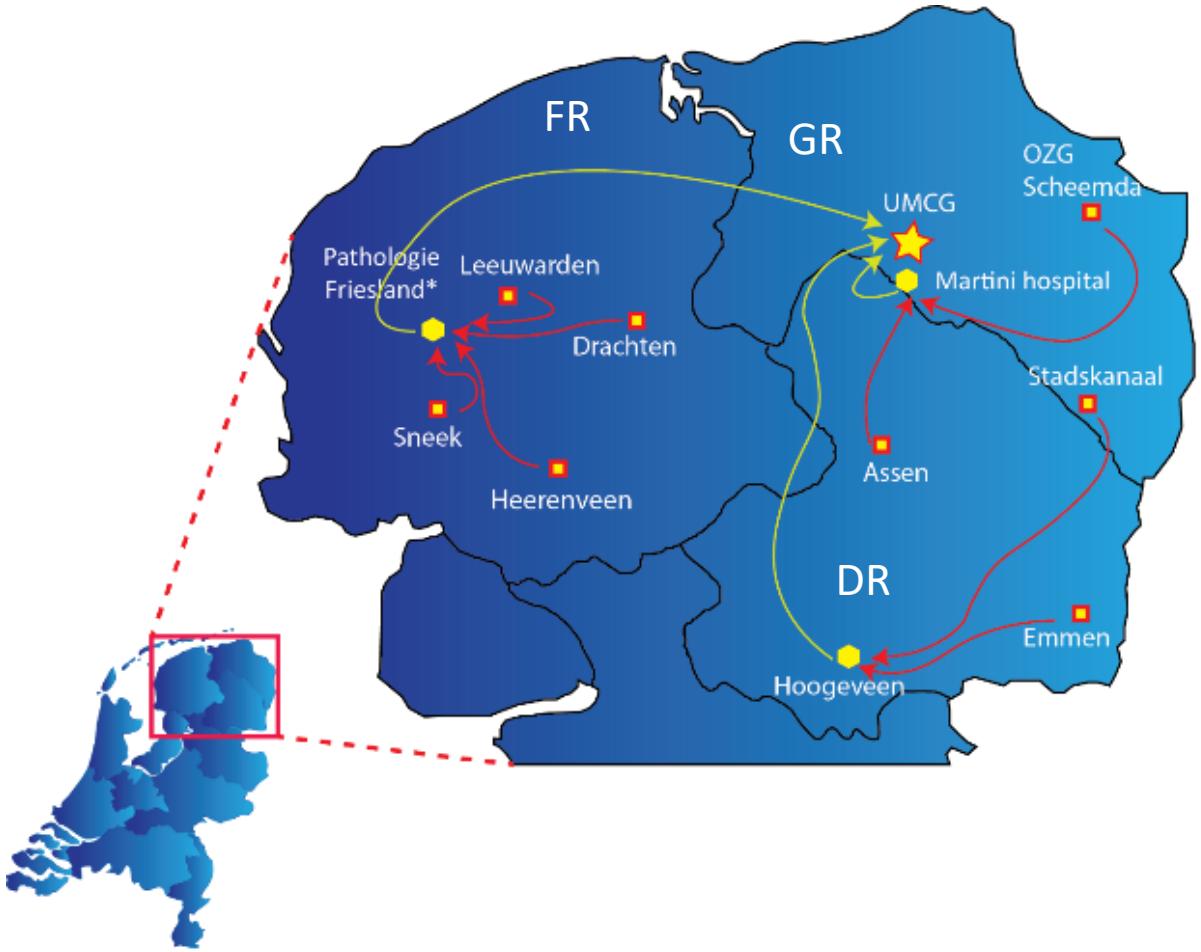
Centralisatie MolD in Noord Nederland

GR:	Groningen	2,960 km²
FR:	Friesland	5,740 km²
DR:	Drenthe	2,680 km²
		11,360 km²
		1.7M inwoners

11 ziekenhuizen
4 pathologie laboratoria
1 centrum voor complexe moleculaire diagnostiek

Hoogeveen-UMCG	65 km
Pathologie Friesland–UMCG	63 km

Compleet MolD analyse nsqNSCLC 2019 : 84%
TAT MolD: 90% in 8-10 werkdagen

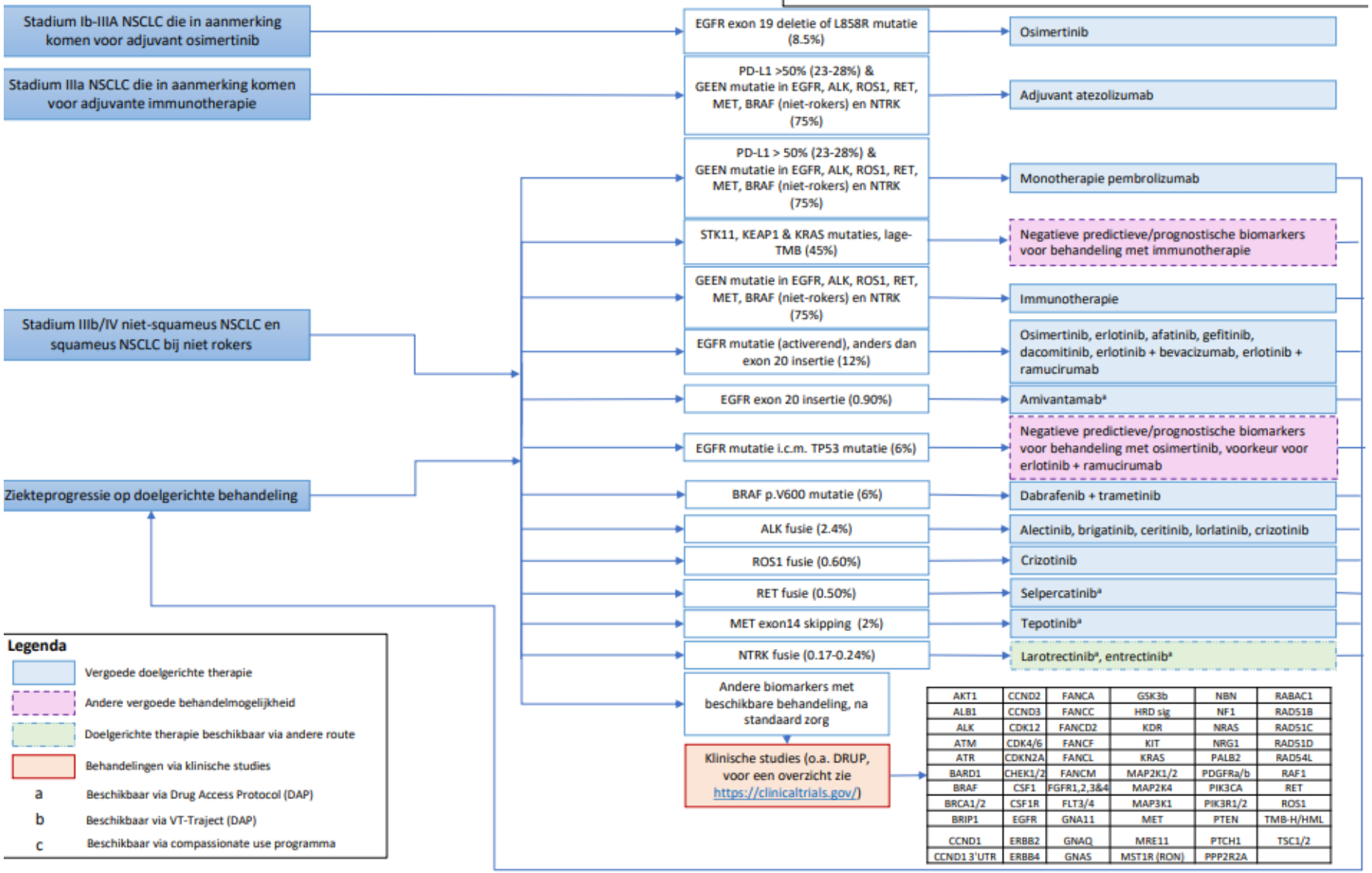


Cajiao Garcia et al. 2023. Submitted

Minimaal Klinisch Noodzakelijke Targets (MKNT-lijst), NL, aug 2023

Niet-kleincellig longcarcinoom (NSCLC)

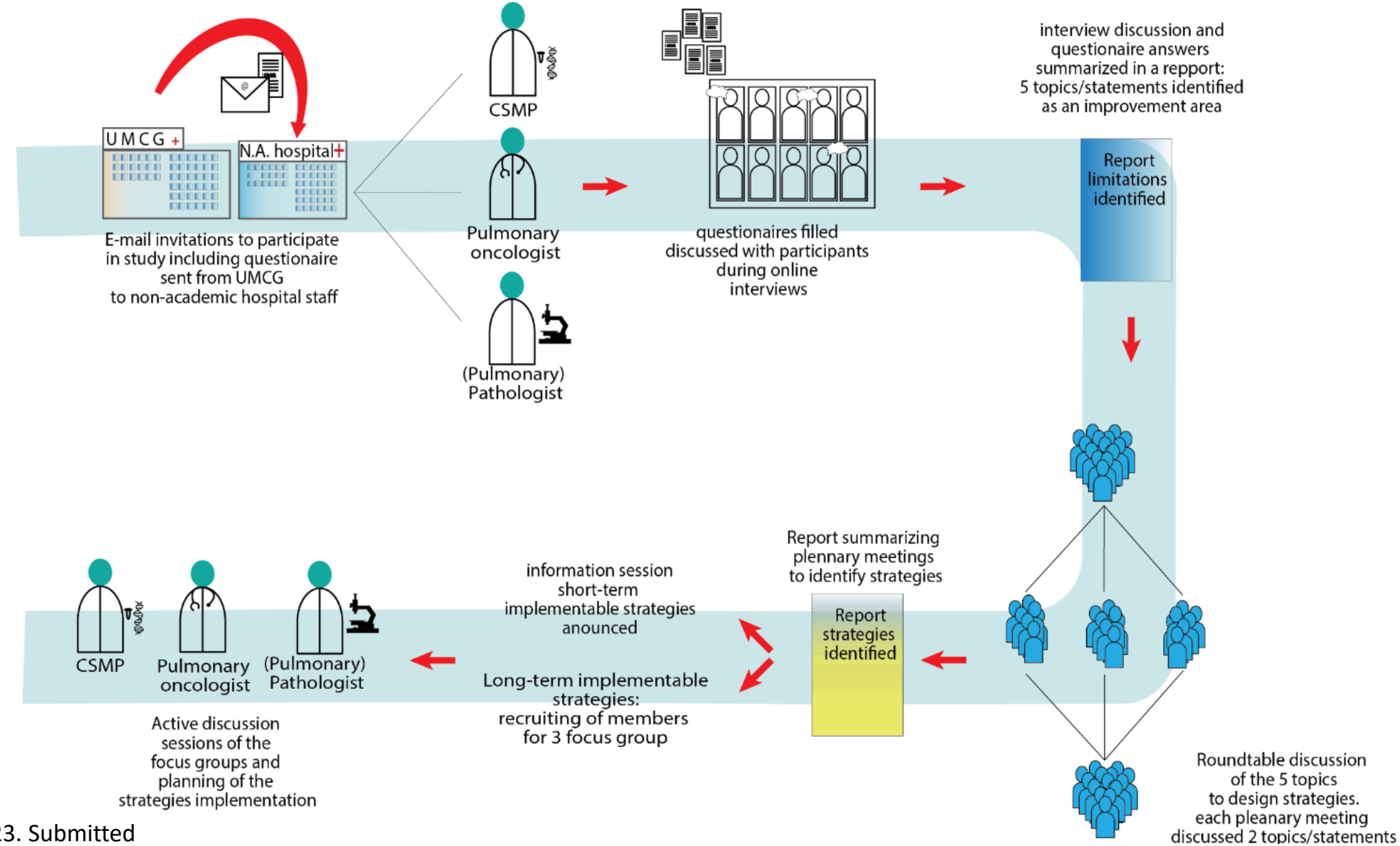
Voor eventuele verwijzing naar klinische geneticus op basis van moleculaire analyse zie
Leidraad voor verwijzing na DNA-onderzoek in (tumor)weefsel | Arts en Genetica
 # Advies voor verwijzing (mogelijk in combinatie met aanvullend criterium)



AKT1	CCND2	FANCA	GSK3b	NBN	RABAC1
ALB1	CCND3	FANCC	HRD sig	NF1	RAD51B
ALK	CDK12	FANCD2	KDR	NRAS	RAD51C
ATM	CDK4/6	FANCF	KIT	NRG1	RAD51D
ATR	CDKN2A	FANCL	KRAS	PALB2	RAD54L
BARD1	CHEK1/2	FANCM	MAP2K1/2	PDGFRa/b	RAF1
BRAF	CSF1	FGFR1,2,3&4	MAP2K4	PIK3CA	RET
BRCA1/2	CSF1R	FLT3/4	MAP3K1	PIK3R1/2	ROS1
BRIP1	EGFR	GNA11	MET	PTEN	TMB-H/HML
CCND1	ERBB2	GNAQ	MRE11	PTCH1	TSC1/2
CCND1 3'UTR	ERBB4	GNAS	MST1R (RON)	PPP2R2A	

Voor referenties en extra informatie zie het begeleidend document van de lijsten Minimaal Klinisch Noodzakelijke Targets (MKNT).
De meest recente versie is te vinden op https://www.nvalt.nl/vereniging/belangrijke-documenten

Interdisciplinair overleg zorgketen longkanker Noord Nederland



Cajiao Garcia et al. 2023. Submitted

Enkele vragen uit de enquête

- When do you request molecular diagnostics?
  - For all stage IIIB/C – IV patients without prior discussion in a multidisciplinary meeting.
  - For all stage IIIB/C – IV adenocarcinoma patients after a multidisciplinary discussion
  - Only for patients with a good performance score
  - I do not request molecular diagnostics. This is the pathologist's task
  - I do not need molecular diagnostics to treat my patients
- For which genes status do you want to know the mutation status for first line targeted therapy?

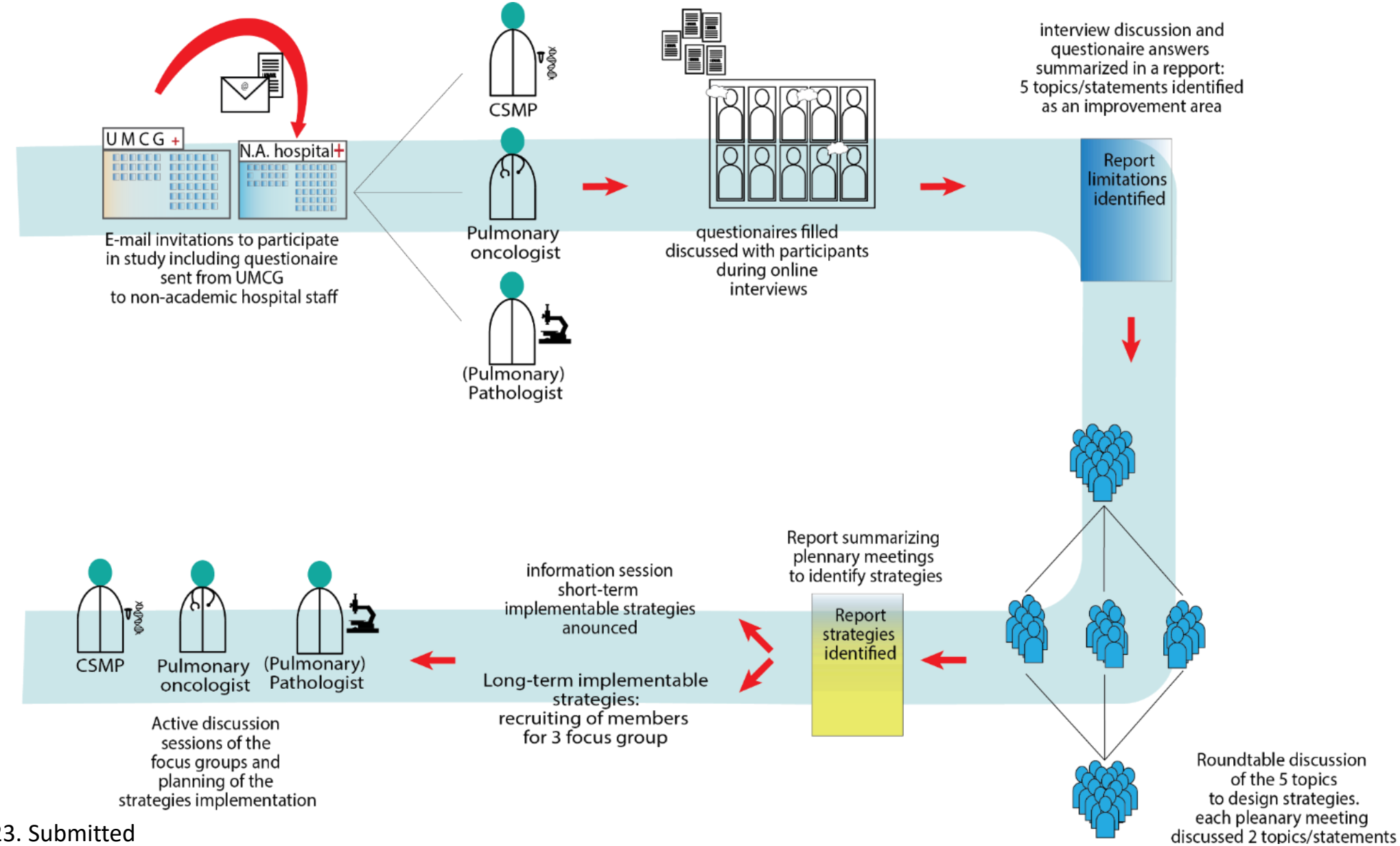
  Always want to know / sometimes want to know / I do not need to know:

  BRAF, EGFR, KRAS, ERBB2, MET exon 14 skipping, ALK translocation, ROS1 translocation, RET translocation, NTRK translocation, NRG1 translocationdiscussion

Enkele vragen uit de enquête

- How do you make sure the pathologist receives sufficient tissue for the analysis?
- What is the percentage of stage IIIB/C-IV patients from whom a proper tissue sample cannot be obtained for predictive analysis?
- In case it is not possible to obtain a good biopsy for mutation analysis, then I:
  - Consider standard chemotherapy, with or without ICI
  - Collect blood for EGFR ctDNA analysis
  - Consult the pathologist/CSMP about the possible alternatives for the obtained material
  - Others, …
- In average, how long (in working days) do you usually wait to receive the pathology report from the moment you obtained the tissue?
- What is an acceptable waiting time (in working days) between the day you obtained the tissue and the date the pathology report was received?
- ……

Interdisciplinair overleg zorgketen longkanker Noord Nederland



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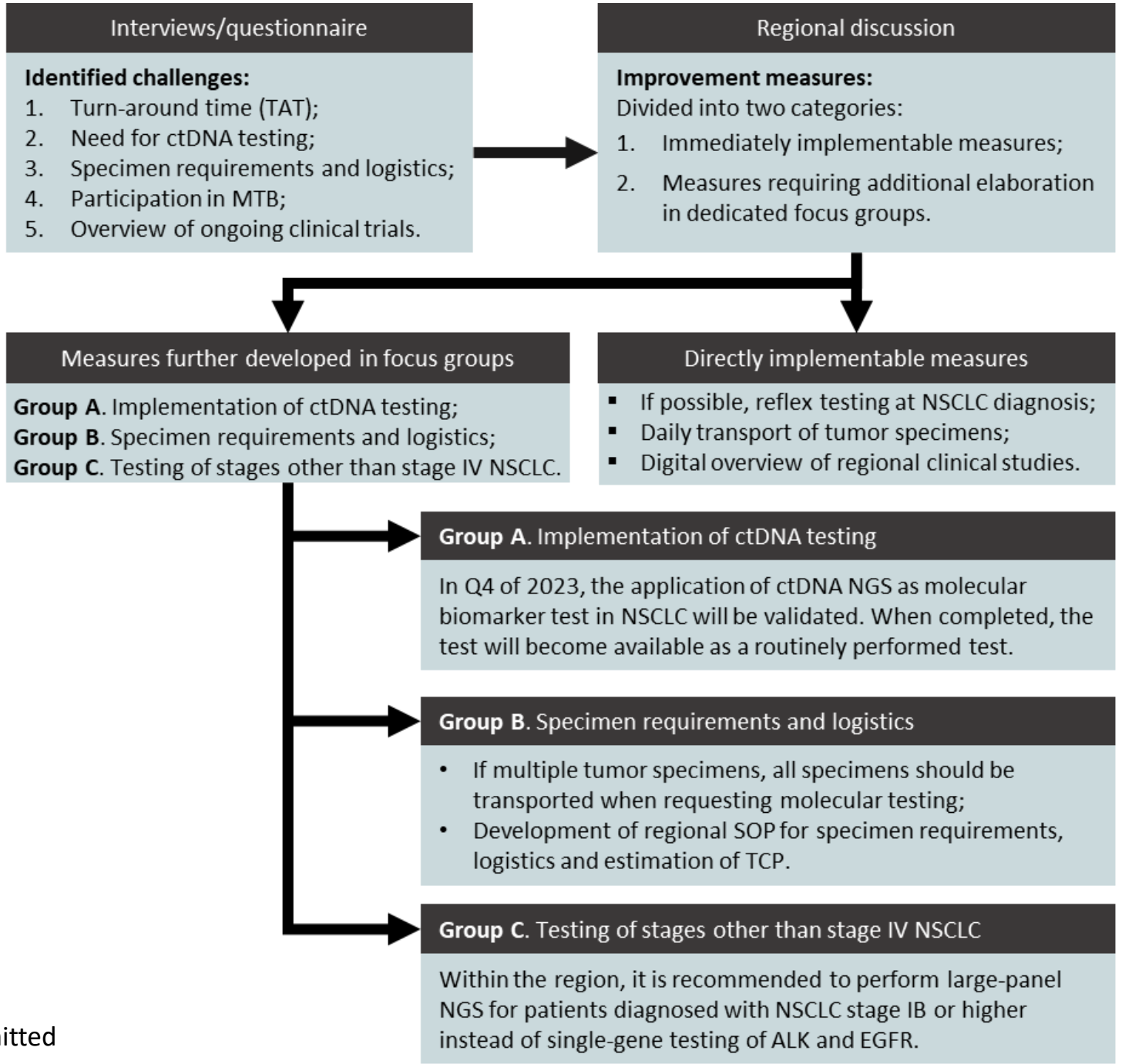

Cajiao Garcia et al. 2023. Submitted

Interdisciplinair overleg zorgketen longkanker, ervaring in Noord Nederland

De Jager et al 2023. *Nederlands Tijdschrift voor Oncologie* 20:70-76

Interdisciplinair overleg zorgketen longkanker

De Jager et al 2023. *Nederlands Tijdschrift voor Oncologie* 20:70-76

Hoe verder in de regio Antwerpen

- Nulpunt meeting MolD NSCLC in België is vooralsnog niet mogelijk.

- Inventarisatie van klinisch relevante behoeften, afstemmen met mogelijkheden binnen de nomenclatuur.
  e.g. *MET* amplificatie

- Gesprekken met een aantal ziekenhuizen in de regio zijn geweest

- Ontwikkelingen
  - CGP analyse → *STK11, KEAP1, TP53, NRG1*, TMB
    € €, langere doorlooptijd, huidige terugbetaling is onvoldoende
  - NGS ctDNA
    € € €, geen terugbetaling (medio 2024?)