CBG MEB
MEDICINES EVALUATION BOARD

Why oncology?

MEB Science Day 2024

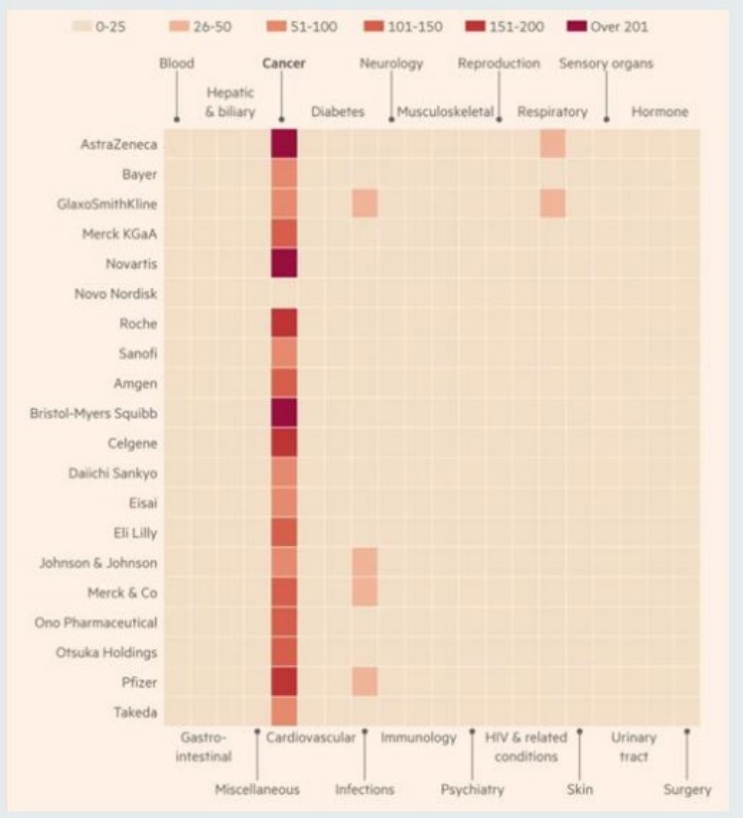
Esther Broekman

clinical assessor MEB - medical oncologist UMCG

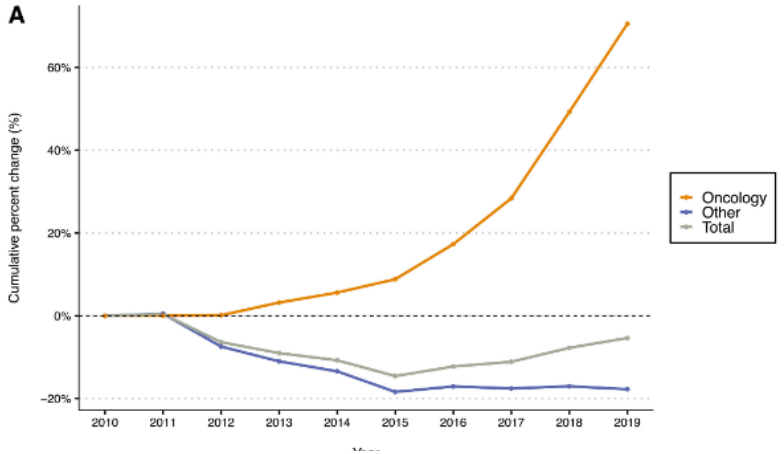
umcg

GOOD MEDICINES USED BETTER

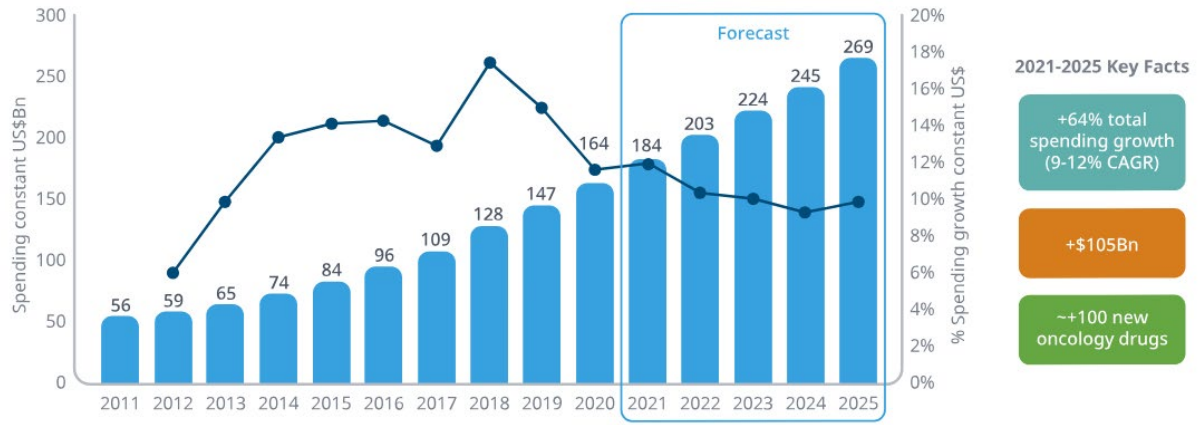
Clinical and societal impact - global



Richard Sullivan, Institute of Cancer Policy, King's College London; Cancer Medicines Forum 5th April 2024



Trends in net revenue from cancer and noncancer drugs from 10 pharmaceutical companies between 2010 and 2019
Meyers et al. Cancer 2021



Source: IQVIA Institute, Feb 2021

Clinical and societal impact - NL

IKNL Rapport Kanker in NL tot 2032

NL: Horizon scan oncology 2024

Horizonscan geneesmiddelen › Geneesmiddelen ›

Oncologie

5 december 2023 | Compacte weergave | Ingedeeld op indicatie

Alvleesklierkanker
- Gemcitabine
- Irinotecan in gepegyleerde liposomen (IND)

Baarmoederhalskanker
- Cadonilimab
- Dostarlimab (IND)

Blaaskanker
- Durvalumab
  - Neo-adjuvant durvalumab met ci (IND)
  - Unresectable locally advanced or (IND)
- Enfortumab vedotin (IND)
- Erdafitinib
- Inbakicept
- Nivolumab (IND)

Borstkanker
- Atezolizumab (IND)
- Capivasertib
- Datopotamab deruxtecan
  - Datopotamab deruxtecan as mor (IND)
  - Datopotamab deruxtecan as mor (IND)
- Elacestrant
- Paclitaxel
- Palbociclib (IND)
- Ribociclib
  - Extension of indication to include (IND)
  - Ribociclib With Endocrine Therap (IND)
- Sacituzumab govitecan (IND)
- Trastuzumab deruxtecan
  - Enhertu as monotherapy is indicated ... (IND)
  - Enhertu as monotherapy is indica (IND)
  - Extension of indication for Enher (IND)
  - Extension of indication to include (IND)
- Trastuzumab duocarmazine

Darmkanker
- Eflornithine / sulindac
- Fruquintinib
- Pembrolizumab / favezelimab
- Trifluridine / tipiracil (IND)

Eierstokkanker
- Dostarlimab (IND)
- Mirvetuximab soravtansine
- Rucaparib (IND)

Hersenkanker
- Dabrafenib / trametinib

Hoofd- en halskanker
- Atezolizumab (IND)
- Leukocyte interleukin
- Tislelizumab (IND)
- Xevinapant

Longkanker
- Adagrasib
- Alectinib (IND)
- Amivantamab
  - Amivantamab in combination wi (IND)
  - Amivantamab in combination with ch...
  - Amivantamab in combination wi (IND)
- Atezolizumab
  - Atezolizumab subcutaneous in pa (IND)
  - Neoadjuvant atezolizumab with c (IND)
- Aumolertinib (mesilate)
- Cemiplimab (IND)
- Datopotamab deruxtecan
  - Datopotamab deruxtecan, in com (IND)
  - Previously Treated Advanced or Meta...
- Domvanalimab
- Durvalumab
  - Imfinzi in combination with trem (IND)
  - Lokaal gevorderd, niet-resectabe (IND)
  - Limited stage small cell lung canc (IND)
- Ipilimumab (IND)
- Lazertinib
- Nintedanib (C)
- Nivolumab (IND)
- Osimertinib
  - Osimertinib in combination with (IND)
  - Stage III unresectable Epidermal (IND)
- Pembroliuzmab (IND)
- Pembrolizumab
  - KEYTRUDA as monotherapy is in (IND)
  - Extension of indication to include (IND)
- Selpercatinib (IND)
- Serplulimab
- Sugemalimab
- Tislelizumab
  - 2L NSCLC (mono): As monotherapy fo...
  - 1L non-squamous NSCLC (combi): In ...
  - 1L squamous NSCLC (combi): In com...
- Toripalimab (IND)
- Trastuzumab deruxtecan (IND)
- Tremelimumab

Maagkanker
- Catumaxomab
- Domvanalimab
- Pembrolizumab
  - Extension of indication for treatm (IND)
  - Extension of indication to include (IND)
  - Treatment in the neoadjuvant or (IND)
- Tislelizumab (IND)
- Trastuzumab deruxtecan (IND)
- Zolbetuximab

Nierkanker
- Atezolizumab (IND)
- Belzutifan
- Ilixadencel

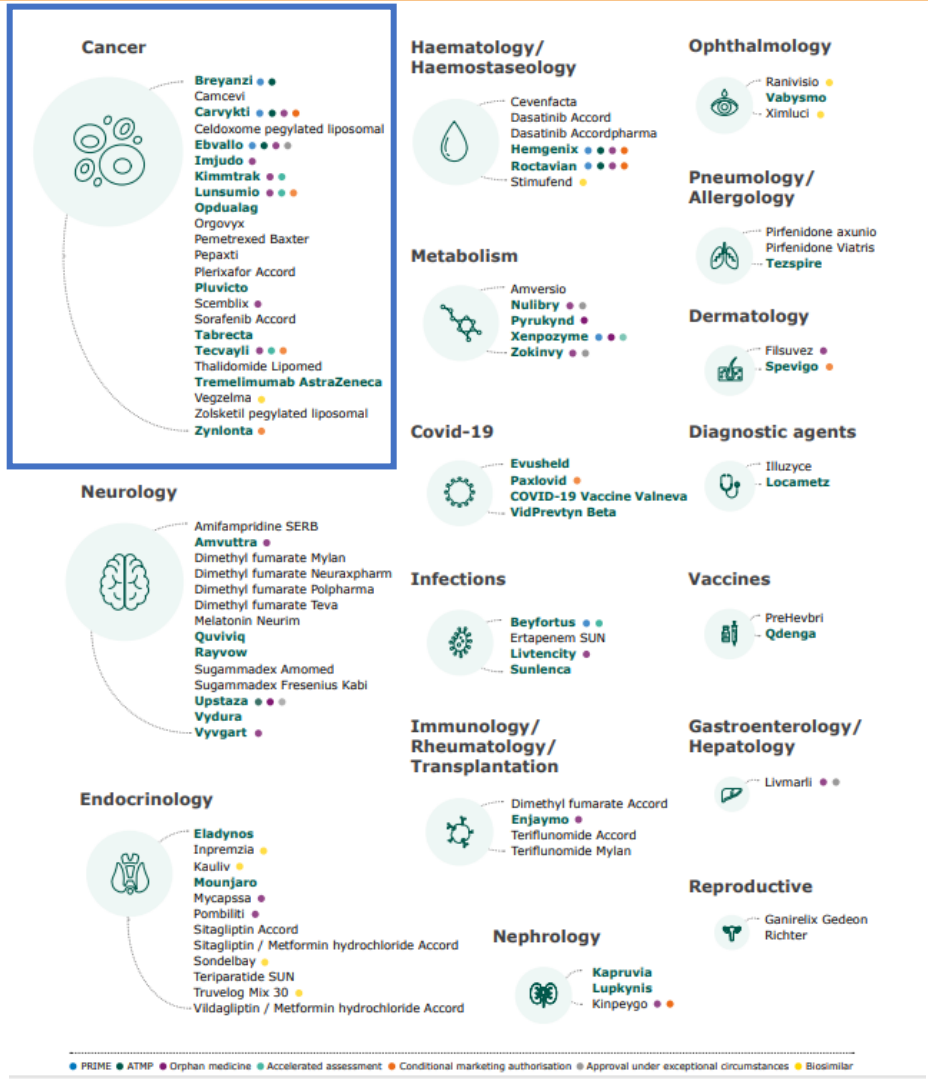
Onbekend
- Binimetinib/encorafenib (IND)
- Olaparib (IND)
- Pembrolizumab (IND)

Oncologie, overig
- AL102
- Afamitresgene autoleucel
- Durvalumab (IND)
- Efbemalenograstim alfa
- Entrectinib (IND)
- Futibatinib
- Igrelimogene litadenorepvec
- Ivosidenib
- Melphalan hydrochloride
- Nirogacestat
- Nivolumab (IND)
- Pembrolizumab (IND)
- Retifanlimab
- Selinexor (IND)
- Sodium thiosulfate
- Tebentafusp
- Tislelizumab
  - Tevimbra as monotherapy is indicate...
  - 1L locally advanced or metastatic ESC...
- Toripalimab
  - Toripalimab combined with cisplatin ...
  - Toripalimab combined with paclitaxel...

Prostaatkanker
- Atezolizumab (IND)
- Darolutamide (IND)
- Degarelix (C)
- Enzalutamide (IND)
- Gozetotide
- Lutetium (177lu) vipivotide tetraxetan
- Niraparib (IND)
- Niraparib / abirateron
- Olaparib (IND)
- Rucaparib (IND)
- Talazoparib (IND)

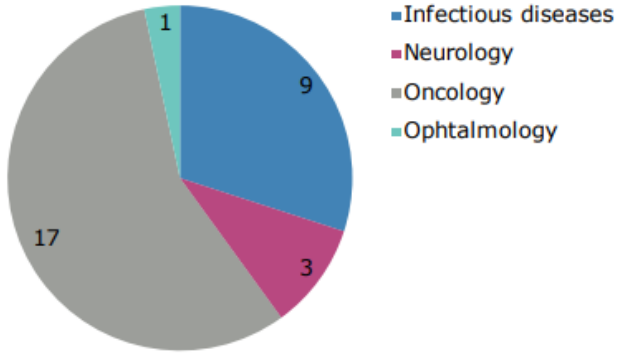
Schildklierkanker
- Selpercatinib
  - Extension of indication to include (IND)
  - Retsevmo is als monotherapie ge (IND)

Regulatory impact



EMA annual report 2022

Figure 5. Conditional marketing authorisations by the therapeutic area (N=30)



CMAs 2006-2016, EMA/471951/2016

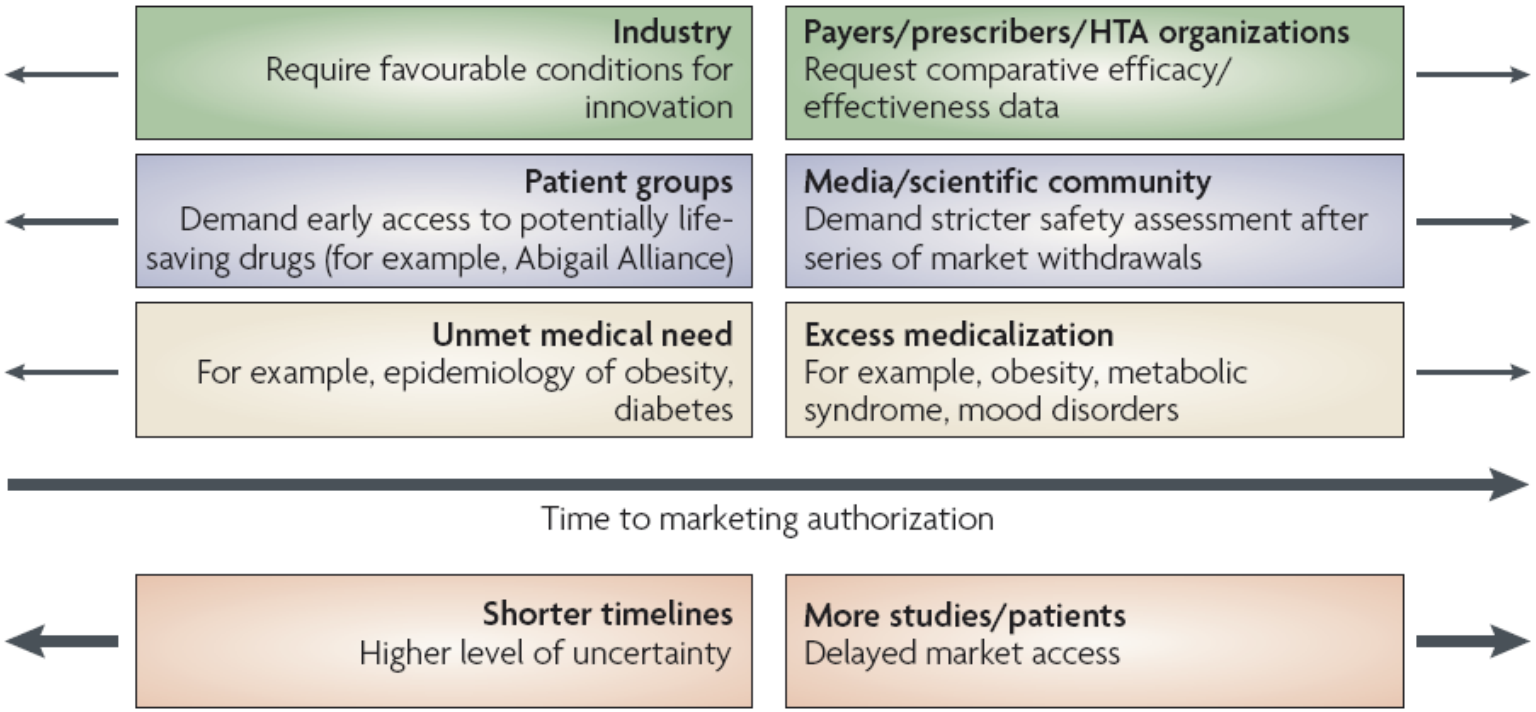
Why oncology?

Field with the **largest impact** from a clinical, societal, regulatory and industry perspective

At the **forefront** of development

At the forefront of clinical and regulatory **issues**, with large societal impact

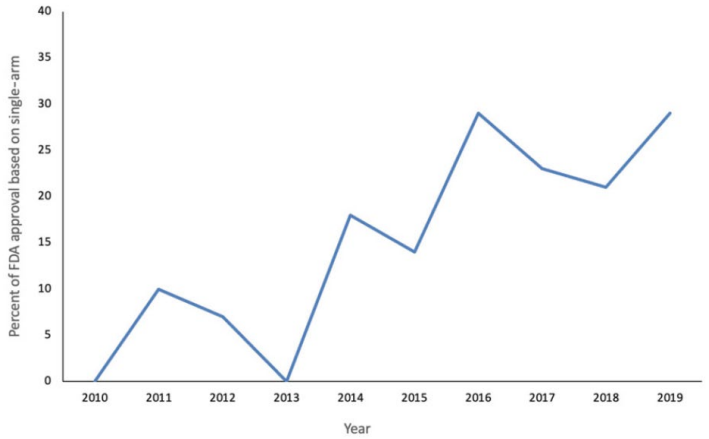
High ‘unmet medical need’ – earlier assessment



Examples of regulatory issues

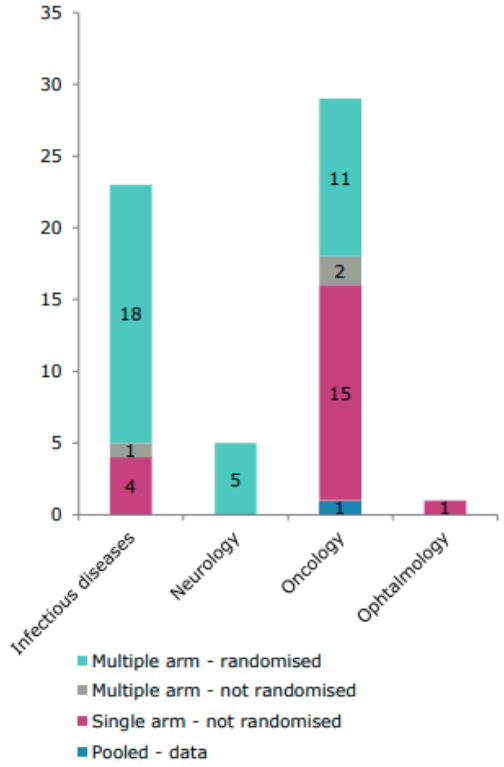
Small populations

- Common disease (lung cancer) becomes rare disease (ALK, ROS, NTRK, RET)
- Single arm trials
- Conditional marketing authorisations
- Less comprehensive data = dealing with **uncertainties**



Rittberg et al. JNCI Cancer Spectrum 2021

Figure 16. Study designs per therapeutic area (N=58)



CMAs 2006-2016, EMA/471951/2016

Examples of regulatory issues

Biomarker driven treatments

- Which population: biological rationale for biomarker versus investigated population
- Validity of biomarker

Trial	Tumour site	Comparison	PD-L1 assay	PD-L1 cut-off for primary endpoint
CheckMate-067[14]	Melanoma	Ipilimumab/nivolumab or nivolumab versus ipilimumab alone	TPS	No PD-L1 cut-off
KEYNOTE-042[18]	Lung	Pembrolizumab versus chemotherapy	TPS	≥1%, ≥20% and ≥50%
KEYNOTE-048[16]	Head and neck	Pembrolizumab versus cetuximab/ chemotherapy	CPS	≥1, ≥20
KEYNOTE-061[19]	Gastric	Pembrolizumab versus paclitaxel	CPS	≥1
KEYNOTE-062[20]	Gastric	Pembrolizumab +/− chemotherapy versus chemotherapy	CPS	≥1
JAVELIN-100[21]	Bladder	Avelumab maintenance after chemotherapy versus no maintenance	Hybrid score	PDL-1 positive by any of several criteria, total population
KEYNOTE-045[13]	Bladder	Pembrolizumab versus chemotherapy	CPS	≥10 and total population
KEYNOTE-355[17]	TNBC	Pembrolizumab + chemotherapy versus chemotherapy	CPS	≥1 and ≥10
IMpassion-130[4]	TNBC	Atezolizumab + nab-paclitaxel versus nab-paclitaxel	IC	≥1% and total population
KEYNOTE-426[23]	RCC	Pembrolizumab + axitinib versus sunitinib	CPS	No PD-L1 cut-off
CheckMate-214[24]	RCC	Ipilimumab/nivolumab versus sunitinib	TPS	No PD-L1 cut-off

Fundytus et al, Ann Oncol 2021

Companion diagnostics ('in vitro diagnostics')

The **In Vitro Diagnostic Devices Regulation** (Regulation (EU) 2017/746) introduces a new classification system for companion diagnostics and the obligation to undergo a conformity assessment by a notified body.

The Regulation applies from 26 May 2022, following a five-year transition period.

Examples of clinical issues

Which **patient**

- Which population: biological rationale for biomarker versus investigated population
- Availability of biomarker testing

Which **treatment schedule**

- Earlier versus later line
- Changing treatment landscape during development of new drug
- Approved dose tolerable for less fit ‘real-world’ patients?
- Treatment optimisation (dose, schedule, duration)

Societal impact

thebmj

High cost oncology drugs without proof of added benefit are burdening health systems

Research into rational use of expensive oncology drugs in clinical practice can benefit health systems and patients

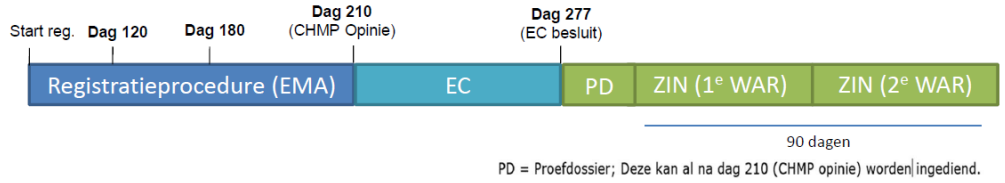
Francine Brinkhuis,[1] Wim G Goettsch,[1,2] Aukje K Mantel-Teeuwisse,[1] Lourens T Bloem[1]

Solutions – collaborations for alignment

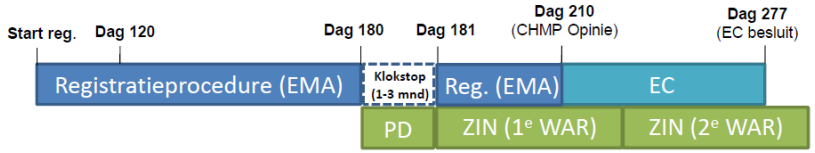
Clinical practice
Other regulatory agencies
HTA organisations

Towards a permanent collaboration framework for EMA and Health Technology Assessment bodies

15 September 2023



Parallelle procedures



Solutions – predictive biomarkers

Organoids

Organoids in (pediatric) cancer research
Dr. Jarno Drost

Organ-on-chip

Regulatory Perspectives on Organ-on-chip models
Dr. Sonja Beken

Precision medicine

Data-driven childhood cancer precision medicine and research
Dr. Patrick Kemmeren

Solutions – early assessment and approval

Dealing with uncertainties

Evidence for regulatory decision-making: when is it considered comprehensive?
Dr. Lourens Bloem

Registry data

Registry data to support regulatory decisions in oncology: More-EUROPA's first experiences with DICA data, minimal data set and outcome of different dosing strategies in clinical practice
Prof. Peter Mol

Postmarketing treatment optimisation

Efficient use of CDK4/6 inhibitors in advanced breast cancer: the SONIA study
Prof. Gabe Sonke

Solutions – collaborate in regulatory science

4) The nature of uncertainties on the benefit-risk balance of anticancer medicines at initial marketing authorisation in the European Union

Anne C. Taams[1,2], Carla A. Herberts[1,3], Anto
Lourens T. Bloem[2]

5) Risk Management of Authorised Advanced Therapy Medicinal Products in the EU

M.J.M Straus[2,3], Helga Gardarsdottir[1,4,5], Marie L. De Bruin[1]

12) Real-world overall survival after alternative dosing for pembrolizumab in the treatment of non-small cell lung cancer: a nationwide retrospective cohort study with a non-inferiority primary objective

Geeske F. Grit[1,2], Esmée van Geffen[3], Ruben Malmberg[4,5], Roelof van Leeuwen[4,5], Stefan Böhringer[6,7], Hans J.M. Smit[8], Pepijn Brocken[9], Job F.H. Eijsink[10], Esther Dronkers[3], Pim Gal[3], Eva Jaarsma[3], Regine J.H.M. van Drie-Pierik[11], Anne M.P. Eldering-Heldens[12], A.N. Machteld Wymenga[13], Peter G.M. Mol[2], Juliëtte Zwaveling[6], Doranne Hilarius[14]

s of targeted anticancer agents
ations

an Bussel[1,2], Steven Teerenstra[1,2], Kit C.B. Roes[1,2]

8) A Natura
Harmonized Communication of Uncertainties Identified during the European Medicine Authorization Process

10) Characterisation of evidence for the correlation of surrogates and clinical outcomes

Renske J. Grupstra[1,2], Elisabeth Bakker[1,2], Viktoriia Starokozhko[1,2,3], Anna M.G. Pasmooij[1,4], Peter G.M. Mol[1,2,5]

13) The potential mismatch between dose recommendations for protein kinase inhibitors and the clinical practice

Margot Brinkhof [1], Sieta T. de Vries[1,2], Peter G.M. Mol[1,2], Marije de Jong[3], Esther Broekman[1,4]

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