Scottish
Cancer Network

NHS
SCOTLAND

Workshop 2: Real World Data and Value Based healthcare in Cancer.

Jonathan Hicks, Clinical Oncologist, Beatson Cancer Centre.

Julie Clarke, Lead Pharmacist, Cancer Medicines Outcome Programme (CMOP).

Real World Evidence and Value Based Health Care

Dunblane 8th March 2024

Jonathan Hicks

Consultant Clinical Oncologist 20 year

Co Chair NDC 1 year

Value of HTA – believer (some US figures later)
Ability to negotiate
SMC Remit and Function
Price Challenges
Price v Value
How to strengthen the process ?
Follow Government lead in terms of balance

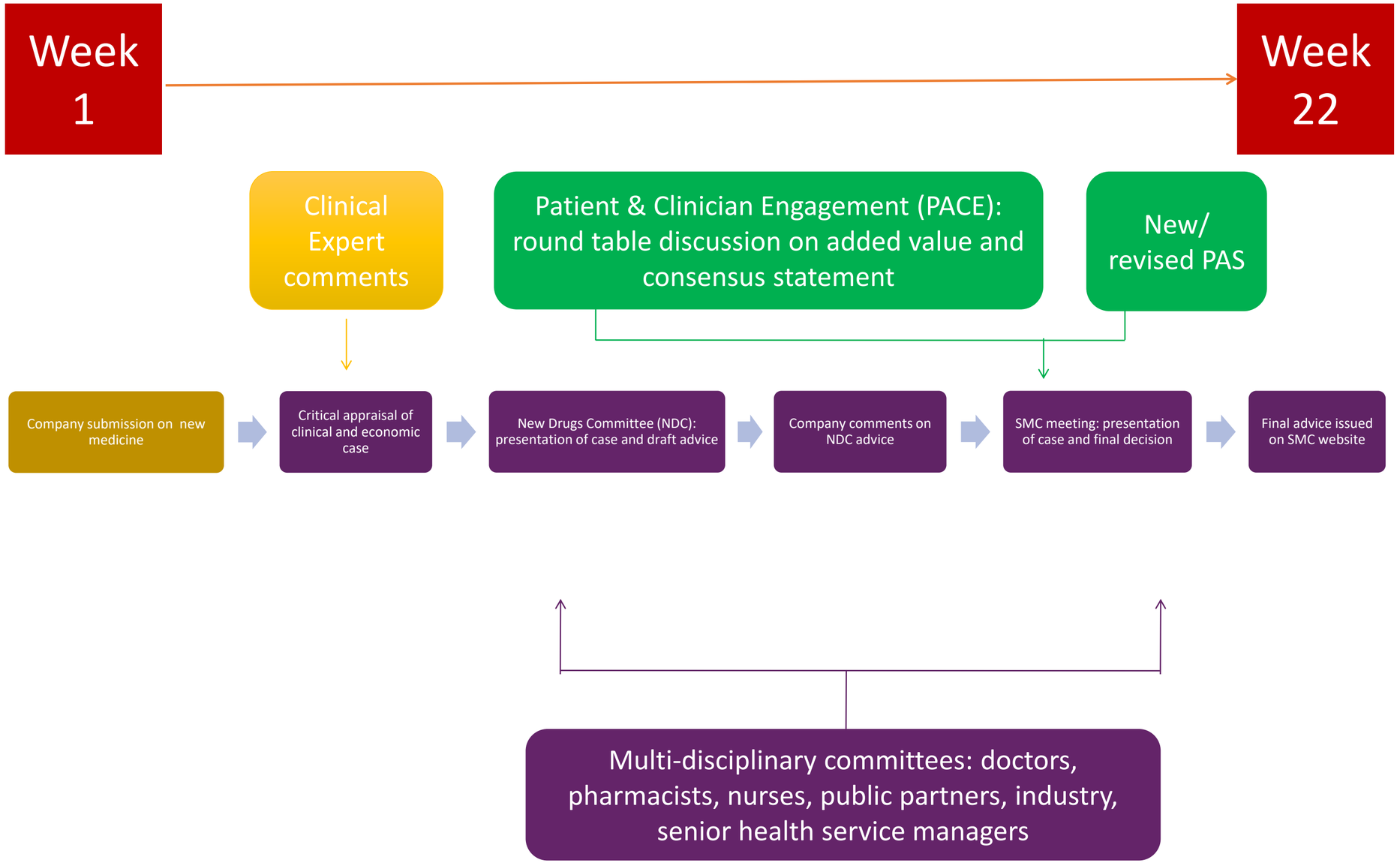
1) Scottish population early access to new medicines
2) Protect the tax payer

Mood music Threshold for decisions set by SG

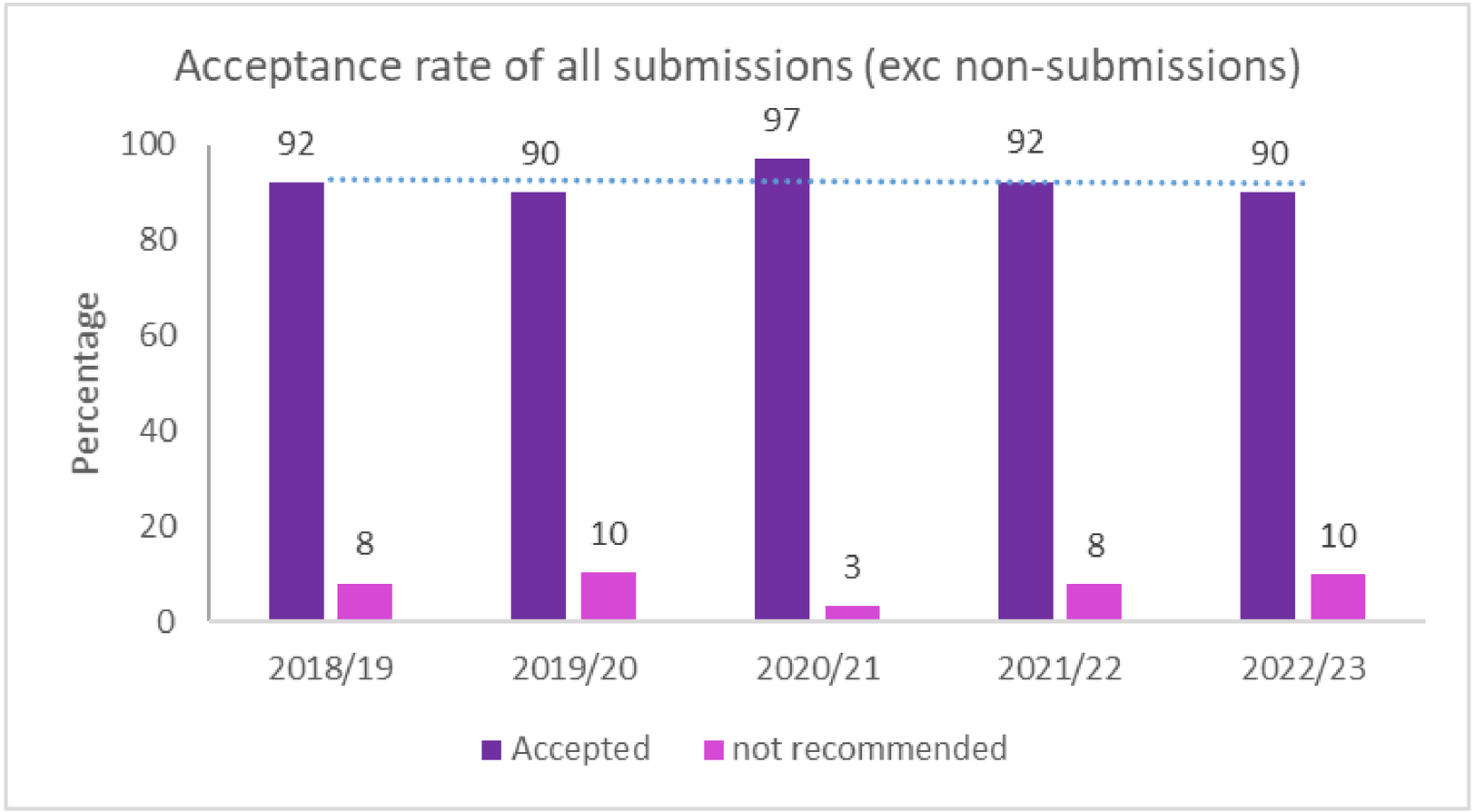
SMC – What they do

- Mandatory feature of HIS core work programme
- ‘Once for Scotland’ new medicines HTA
- Evaluation and provision of advice to the health service on clinical and cost effectiveness
- Support patient group submissions and involvement at PACE meetings (for eligible medicines)
- Two stage process – New Drugs Committee/SMC
- Ensure that medicines offering good value are accepted quickly so that patients can benefit
- Horizon Scanning Function.

How we do HTA (End of Life/Orphan)



Stats: acceptance rates of all submissions (excluding non-submissions)



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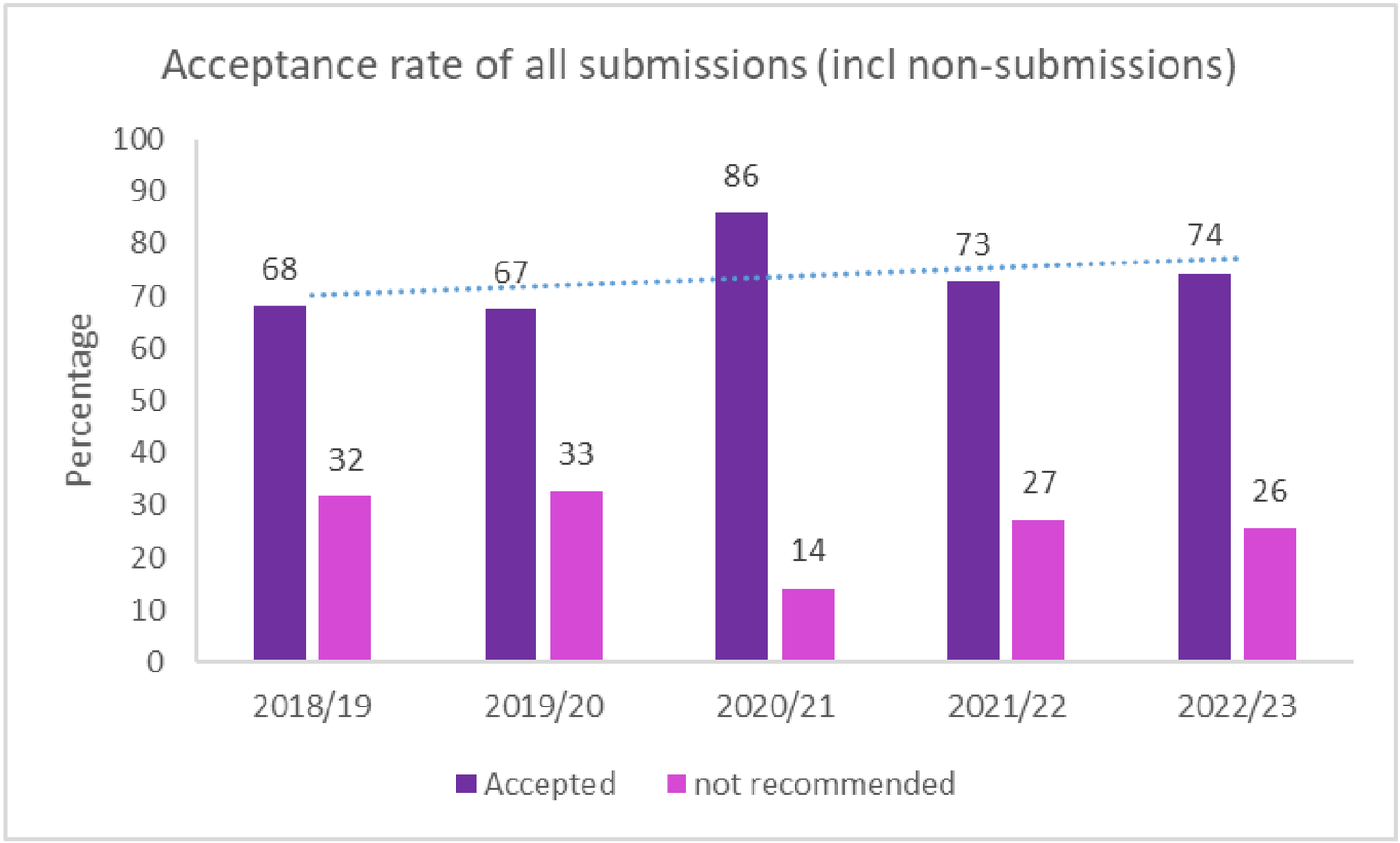
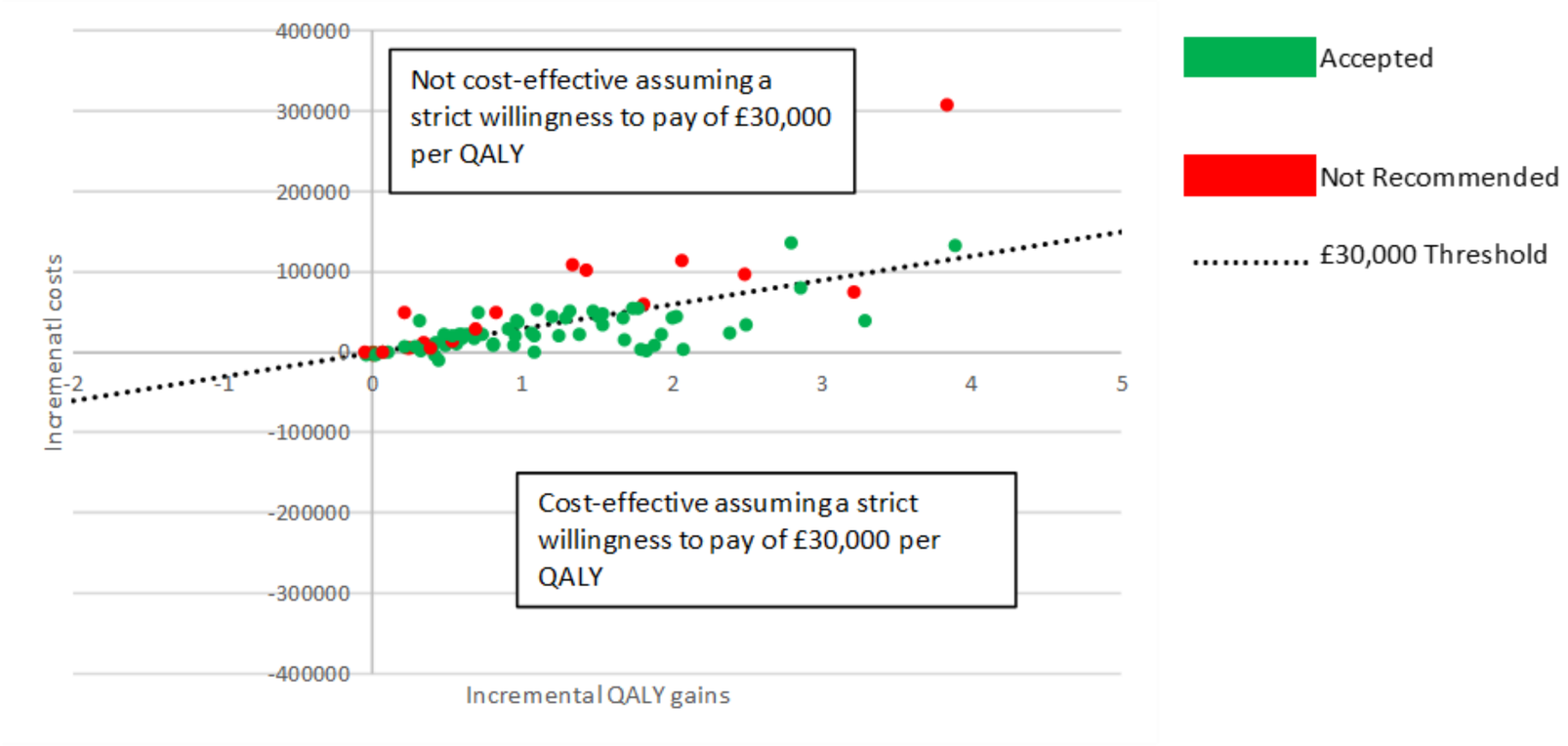


Stats: Cost-effectiveness plane of SMC decision making (decisions published April 2021 to Sept 2023)



<u>Notes:</u> Restricted to cost-utility analysis only. Excluding abbreviated submissions, UO initial assessments and collaborations. Accepted combination of Accepted, Accepted Restricted and Interim Acceptance.

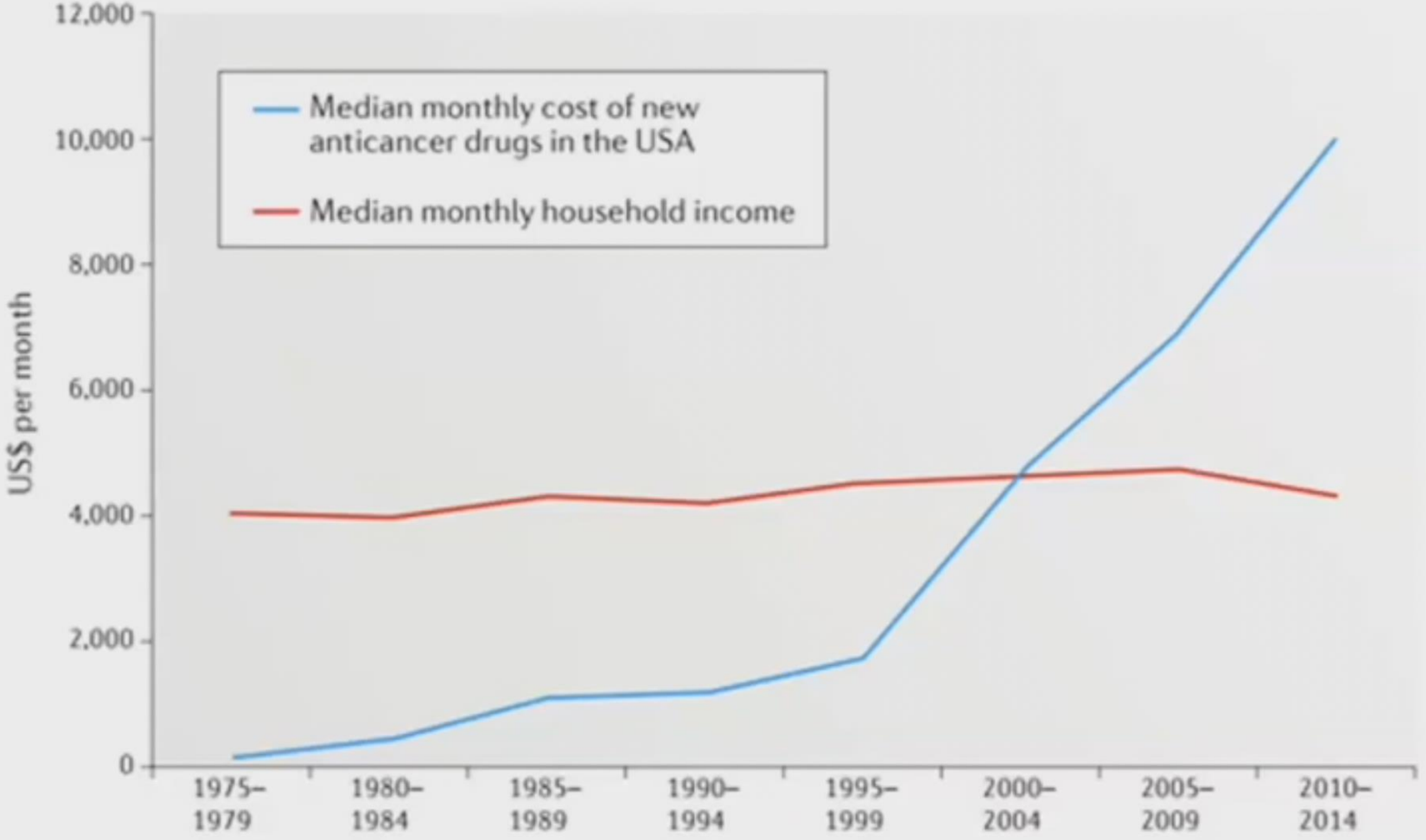
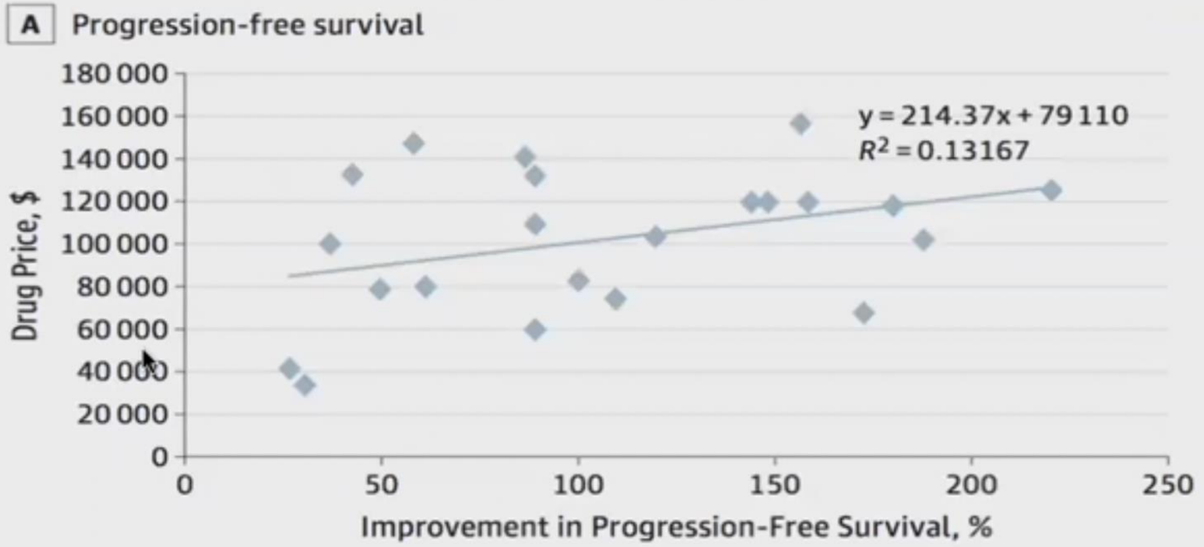
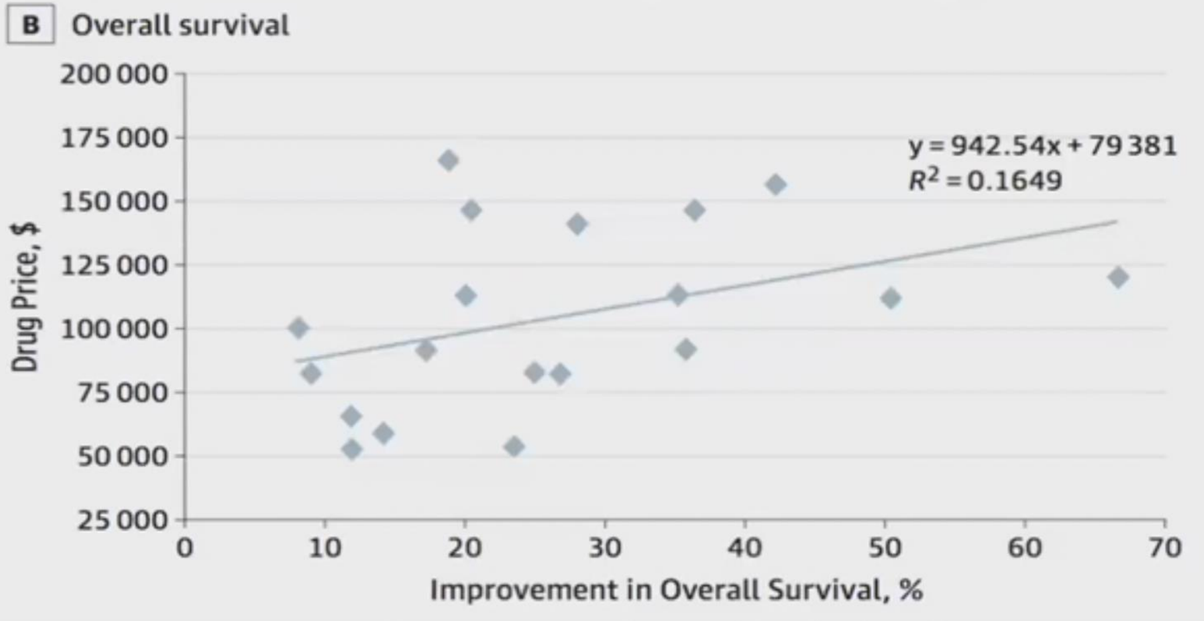


Figure 2 | **Median monthly launch price of a new anticancer drug, compared with median monthly household income from 1975–2014 in the USA.** Data on household incomes were obtained from the 2015 United States Census[130], and drug prices were obtained from Bach & Schnorr[131].

No correlation of price to improvement in outcomes

Figure. Linear Regression Analysis of Drug Price vs Percentage Improvement in Survival

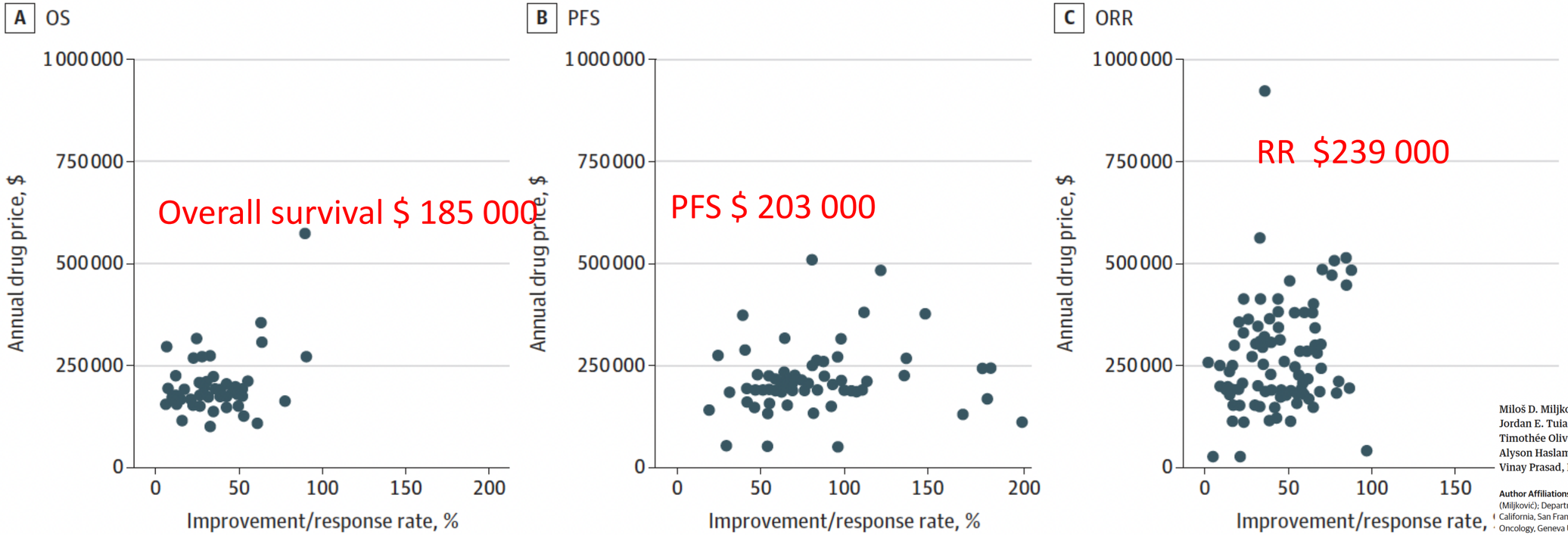




Association Between US Drug Price and Measures of Efficacy for Oncology Drugs Approved by the US Food and Drug Administration From 2015 to 2020

Median annual Price : approval based on ……

Figure. Median Annual Cost by End Point for US Food and Drug Administration Approved Drugs From 2015 to 2020



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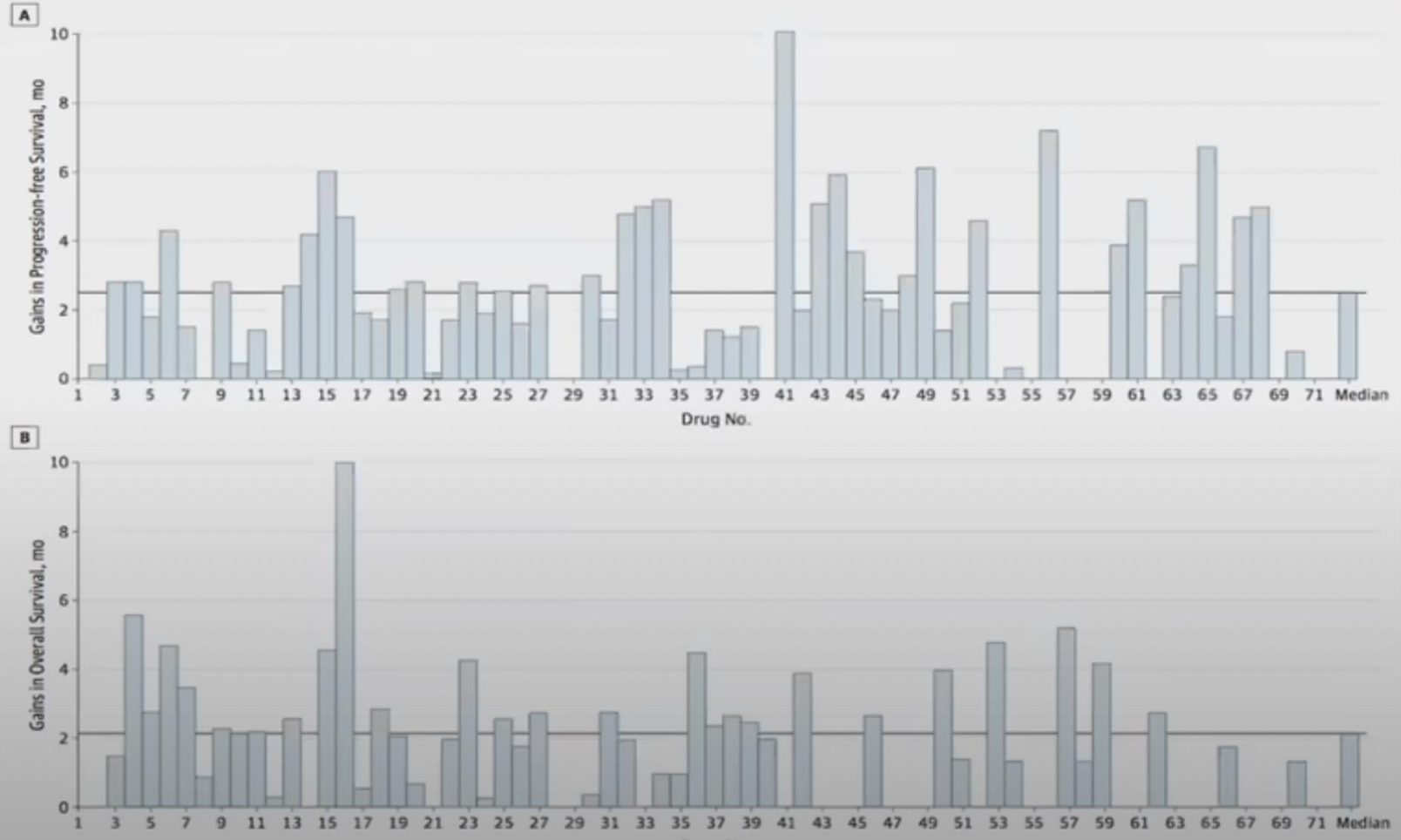
Accepted for Publication: August 18, 2022.

Published Online: October 31, 2022. doi:10.1001/jamainternmed.2022.4924

Average cancer drug approved by FDA improves PFS by 2.3 months – HR sitting 0.6 – 0.8
This on average equates to a 2.1 months improvement in overall survival HR sitting 0.8 -0.9

The average cancer drug

Figure 1. Graphical Representation of the Results in Table 1: Gains in Progression-Free Survival (PFS) and Overall Survival (OS) for the 71 Drugs Approved by the FDA From 2002 to 2014 for Metastatic and/or Advanced and/or Refractory Solid Tumors



DLBCL – example of challenge of data: 2023
Rush to licence

First line

Polatuzumab

R-CHOP v Pola R CHP : RP3: Polarix : swapped out oncovin

Primary endpoint : mPFS PET relapse q 6 weekly

Second line

Polatuzumab + bendamustine + rituximbab: v BR : 80pt

Randomised PH2

Primary endpoint CR

Axicabtegene ciloleucel v SOC: RP3 : 360 pts

Primary end point EFS:

Glofitamab : 155pts

Single arm Ph 2 : RR

Loncastuximab : 145 pts

Single arm Ph 2 :

Tafasitamab + lenalidomide : 80 pts

Single arm Phase 2: Primary End point RR, mPFS, mDOR

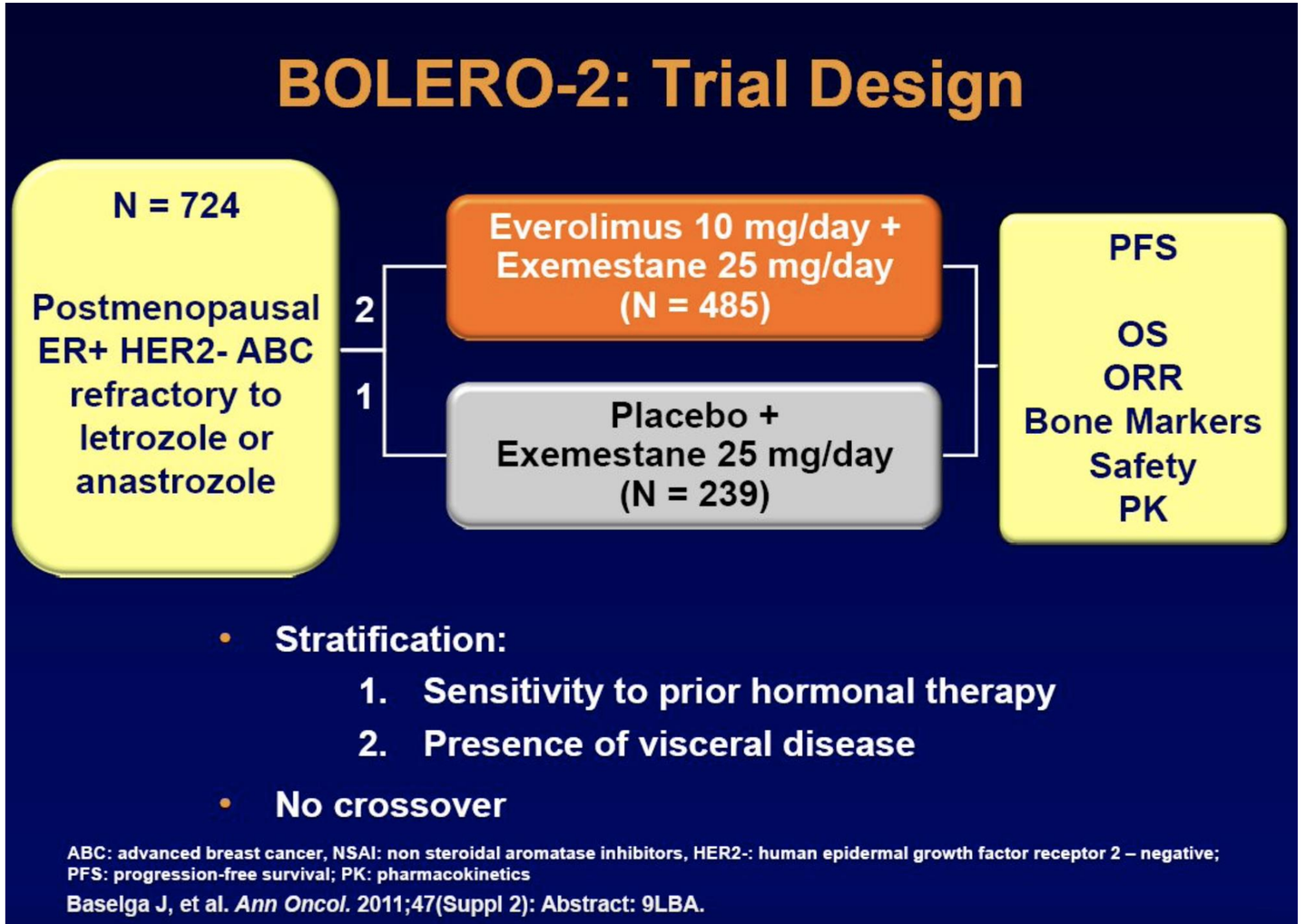
Epcoritamab: 131 pts

Single arm Phase 2: Primary End point RR, mPFS, mDOR

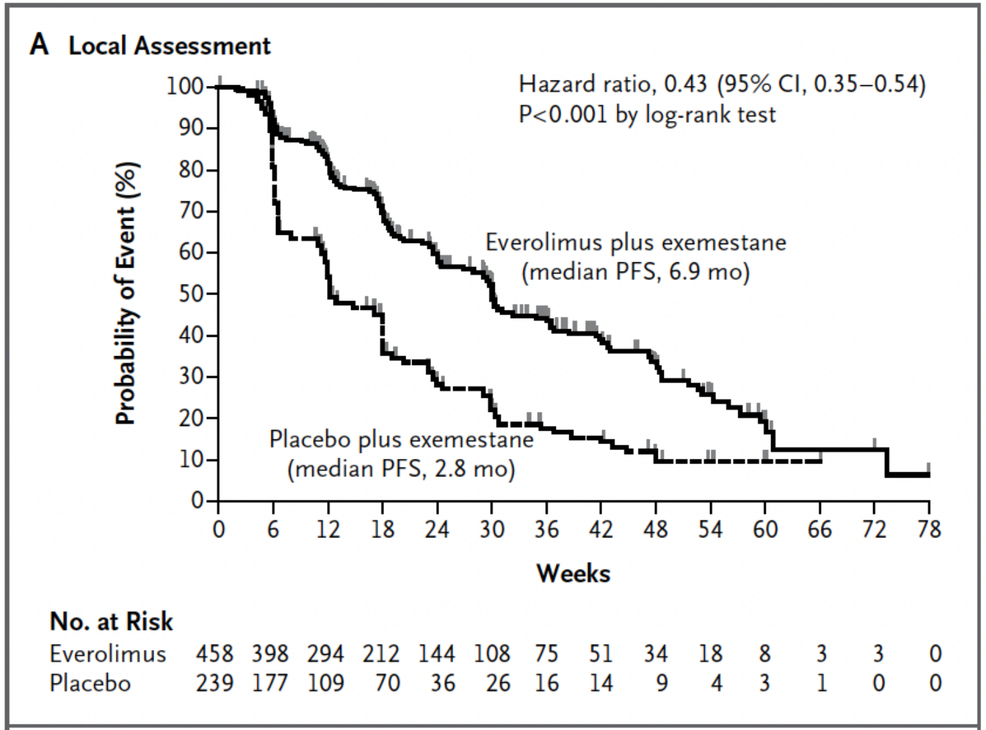
ORIGINAL ARTICLE

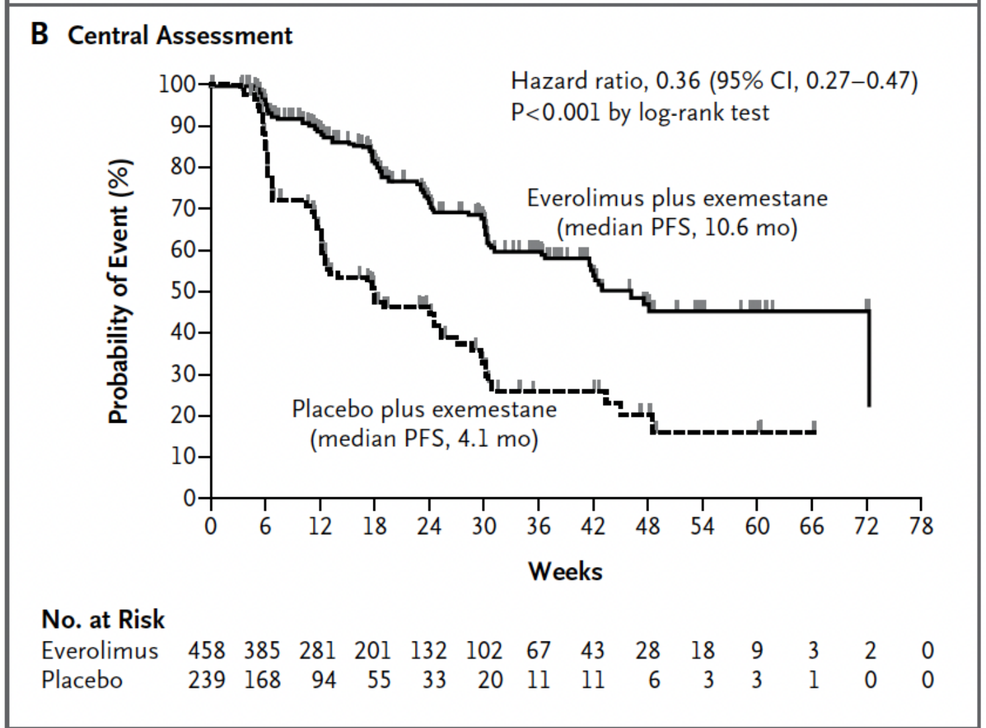
Everolimus in Postmenopausal Hormone-Receptor–Positive Advanced Breast Cancer

José Baselga, M.D., Ph.D., Mario Campone, M.D., Ph.D.,



10.1056/nejmoa1109653 nejm.org





Informed sensoring in treatment arm
Licenced on PFS

2011

Figure 1. Kaplan–Meier Plot of Progression-free Survival.

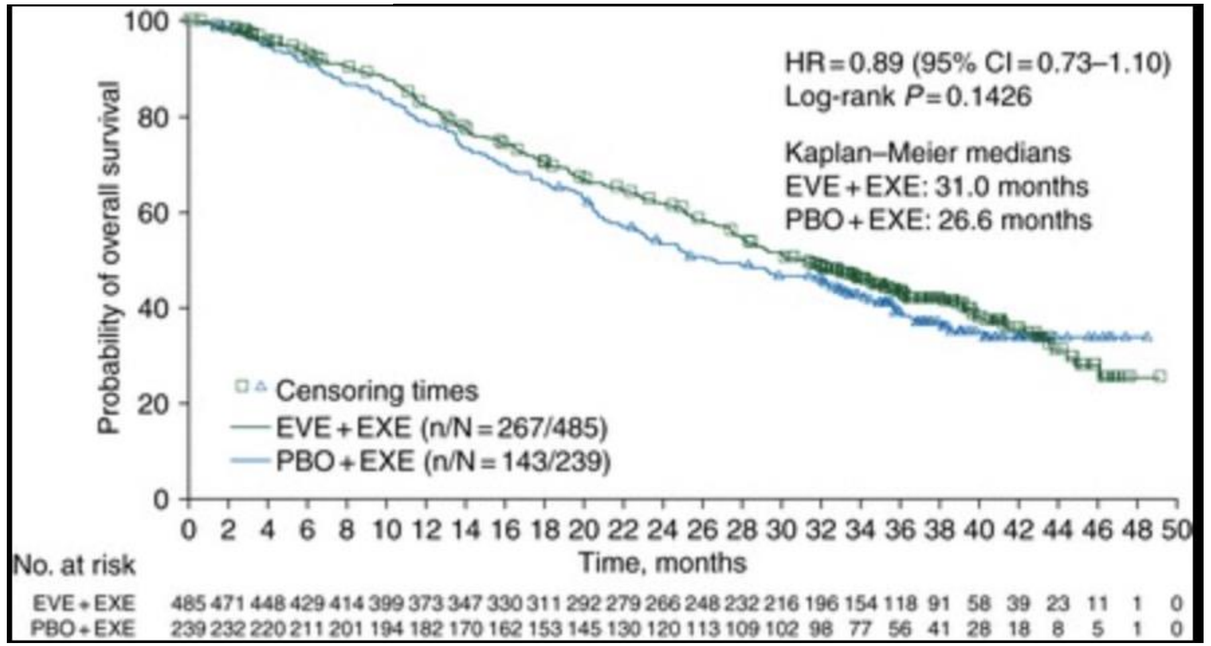
Panel A shows progression-free survival on the basis of local assessment of radiographic studies, and Panel B shows central assessment. PFS denotes progression-free survival.

Clinical Trial > Ann Oncol. 2014 Dec;25(12):2357-2362. doi: 10.1093/annonc/mdu456.

Epub 2014 Sep 17.

Everolimus plus exemestane for hormone-receptor-positive, human epidermal growth factor receptor-2-negative advanced breast cancer: overall survival results from BOLERO-2†

M Piccart [1], G N Hortobagyi [2], M Campone [3], K I Pritchard [4], F Lebrun [5], Y Ito [6], S Noguchi [7], A Perez [8], H S Rugo [9], I Deleu [10], H A Burris 3rd [11], L Provencher [12], P Neven [13], M Gnant [14], M Shtivelband [15], C Wu [16], J Fan [16], W Feng [16], T Taran [16], J Baselga [17]



Ann Oncol 2014 Dec;25(12):2357-2362. doi: 10.1093/annonc/mdu456.

March 2016

Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
www.scottishmedicines.org.uk
Delta House 50 West Nile Street Glasgow G1 2NP Tel 0141 225 6999 Chairman: Professor Jonathan G Fox
NHS SCOTLAND

Resubmission

everolimus 2.5mg, 5mg and 10mg tablets (Afinitor®) SMC No. (872/13)
Novartis Pharmaceuticals UK Limited

04 March 2016

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in Scotland. The advice is summarised as follows:

ADVICE: following a second resubmission assessed under the end of life process:

everolimus (Afinitor®) is accepted for use within NHS Scotland.

WoS audit result of Everolimus

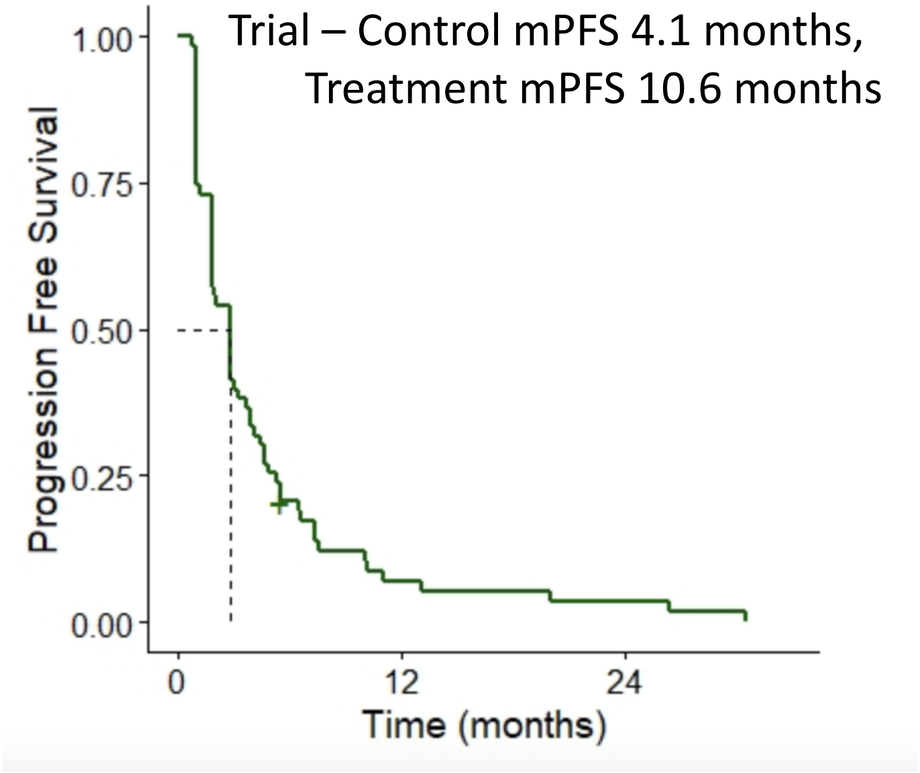
68 patients 2016 – 2022. Declined as a poster by UKBCG in 2022

Time on treatment – surrogate for PFS

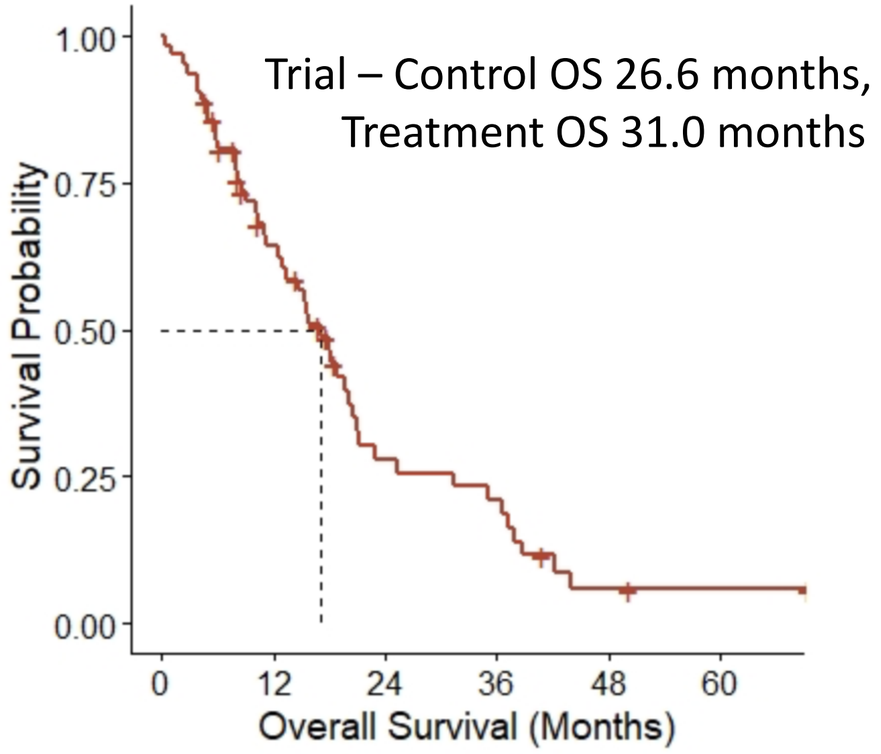
mToT 2.7months

8/62 stopped cycle 1 due to toxicity – if excluded

mToT 3.1 months



Overall Survival : 16.9 months



Sotorasib
Single arm Phase 2 Codebreak 100

2021 March

- RR : 37%
- mPFS : 6.8 months
- mOS: 12.5

SMC Feb 2022 -approved

Scenario analysis

Table 1: Key scenario analyses with PAS

	Base case/Scenario	Base case approach	ICER (£/QALY)
	Base case	**N/A**	**38,715**
1.	Use of Flatiron data for indirect treatment comparison	Use of unanchored MAIC	33,811
2.	15-year time horizon	20-year time horizon	39,696
3.	Log logistic distribution selected to estimate long-term OS and PFS projections	Log-normal distribution for OS and PFS projections	43,529
4.	MAIC-adjusted TTD curve from CodeBreaK100	To test the impact of an alternative approach to estimate long-term treatment duration.	39,454
5.	HR of sotorasib vs. docetaxel = 1 after 5 years	Treatment effect of sotorasib maintained for time horizon	41,377
6.	Apply health state utilities by progression status	Use of time-to-death utilities	41,861
7.	Include drug wastage based on total packs administered (rather than days of tablets received)	Drug wastage based on days of tablets received	41,119
8.	Combined scenario	Combination of: 3, 5, 6, 7	50,079

OS, overall survival; PFS, progression-free survival; TTD, time to treatment discontinuation; HR, hazard ratio; MAIC, matching-adjusted indirect comparison; KM, Kaplan-Meier; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year;

Sotorasib
Codebreak 200
FDA insisted on RP3
2023 – Feb

Interim acceptance – so to be reviewed

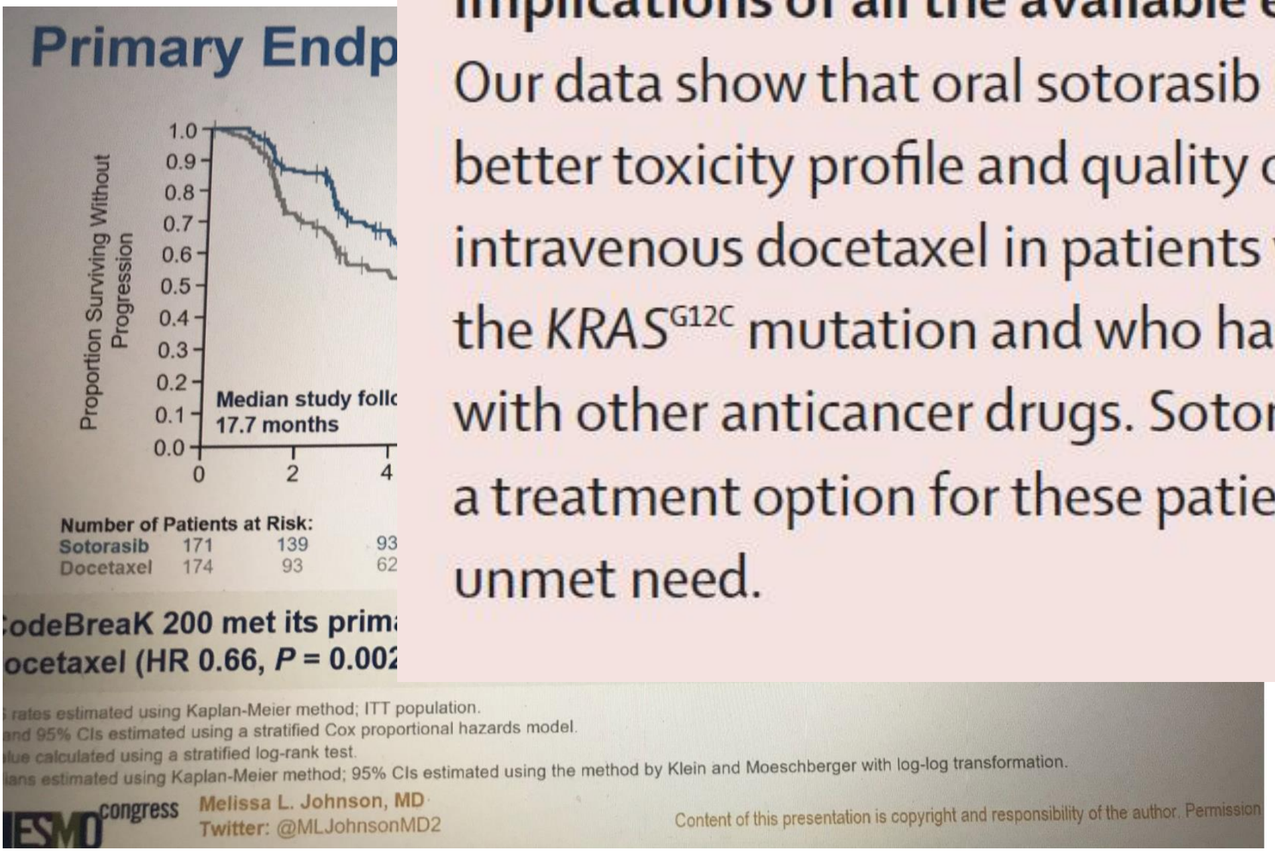
Sotorasib versus docetaxel for previously treated non-small-cell lung cancer with *KRAS*^{G12C} mutation: a randomised, open-label, phase 3 trial

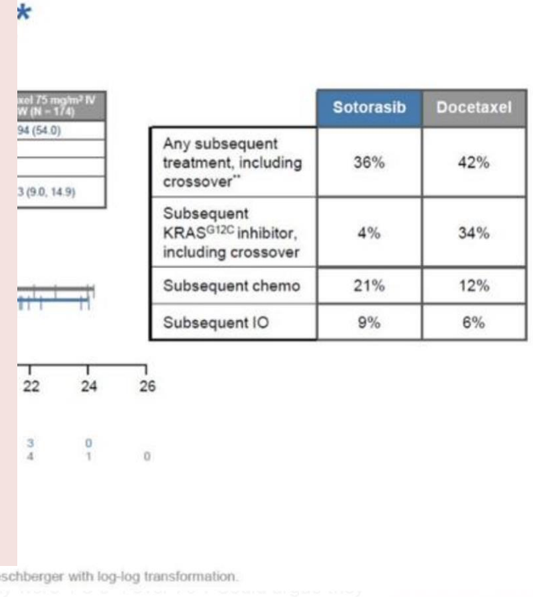
Adrianus Johannes de Langen, Melissa L Johnson, Julien Mazieres, Anne-Marie C Dingemans, Giannis Mountzios, Miklos Pless, Jürgen Wolf, Martin Schuler, Hervé Lena, Ferdinandos Skoulidis, Yasuto Yoneshima, Sang-We Kim, Helena Linardou, Silvia Novello, Anthonie J van der Wekken, Yuanbin Chen, Solange Peters, Enriqueta Felip, Benjamin J Solomon, Suresh S. Ramalingam, Christophe Dooms, Colin R Lindsay, Carlos Gil Ferreira, Normand Blais, Cynthia C Obiozor, Yang Wang, Bhakti Mehta, Tracy Varrieur, Gataree Ngarmchamnanrith, Björn Stollenwerk, David Waterhouse, Luis Paz-Ares*, for the CodeBreaK 200 Investigators†*

PFS: HR 0.66 (5.5 v 4.5) **OS: HR 1.01 ; 11.5 v 10.5 (favour control)**

Implications of all the available evidence

Our data show that oral sotorasib had improved efficacy, with a better toxicity profile and quality of life, compared with intravenous docetaxel in patients with advanced NSCLC with the *KRAS*^{G12C} mutation and who had been previously treated with other anticancer drugs. Sotorasib should be considered as a treatment option for these patients, who have a substantial unmet need.





	Sotorasib	Docetaxel
Any subsequent treatment, including crossover**	36%	42%
Subsequent KRAS^{G12C} inhibitor, including crossover	4%	34%
Subsequent chemo	21%	12%
Subsequent IO	9%	6%

22 24 26

[§]Medians estimated using Kaplan-Meier method; 95% CIs estimated using the method by Klein and Moeschberger with log-log transformation.

Palbociclib 2016

Paloma 2

CK 4/6 – targeted agent – no target

AB v A trials

PFS to OS data 6 years

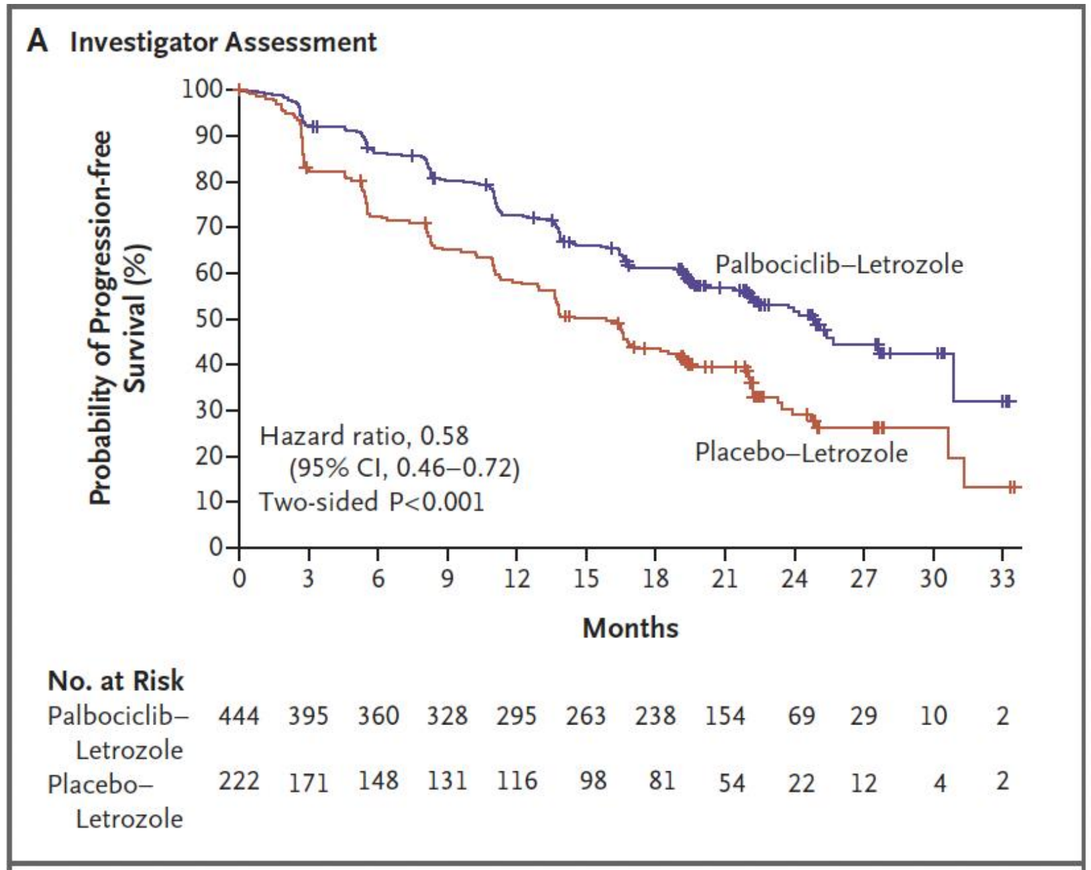
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 17, 2016 VOL. 375 NO. 20

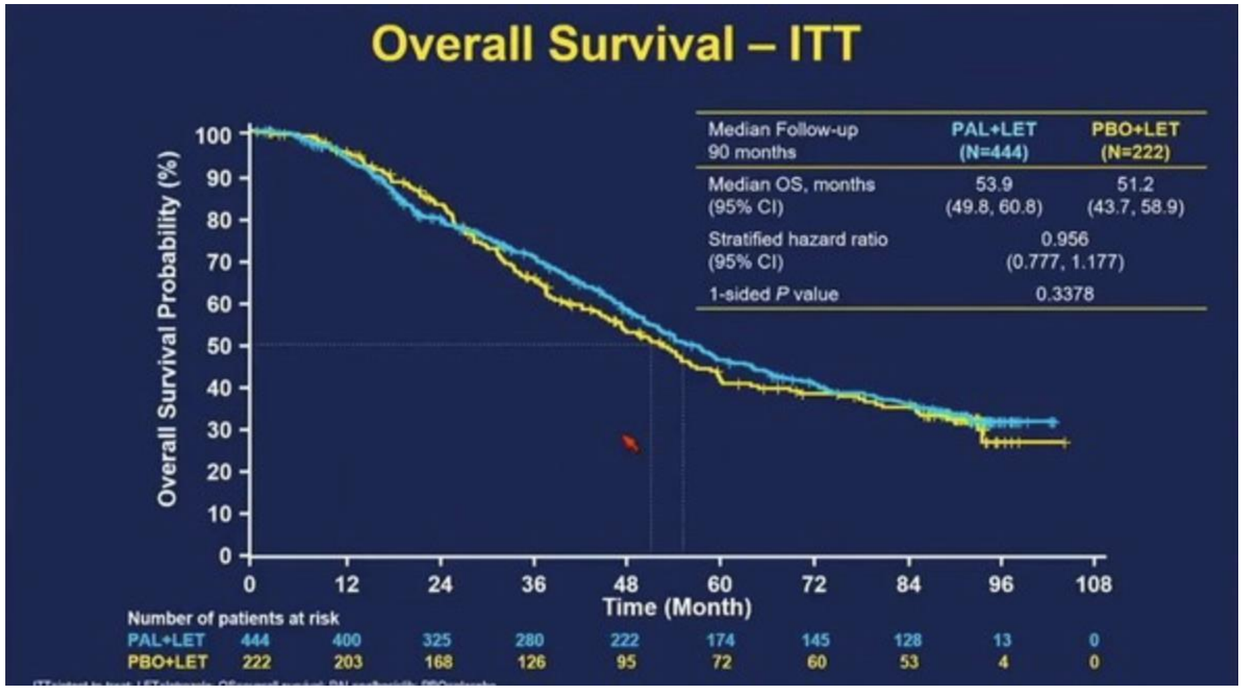
Palbociclib and Letrozole in Advanced Breast Cancer

Richard S. Finn, M.D., Miguel Martin, M.D., Hope S. Rugo, M.D., Stephen Jones, M.D., Seock-Ah Im, M.D., Ph.D., Karen Gelmon, M.D., Nadia Harbeck, M.D., Ph.D., Oleg N. Lipatov, M.D., Janice M. Walshe, M.D., Stacy Moulder, M.D., Eric Gauthier, Pharm.D., Ph.D., Dongrui R. Lu, M.Sc., Sophia Randolph, M.D., Ph.D., Véronique Diéras, M.D., and Dennis J. Slamon, M.D., Ph.D.

HR : 0.58 : 25 v 15 months : RR 42 v 35%



HR 0.96 2022: 54 v 51 months



ARTICLE OPEN

Check for updates

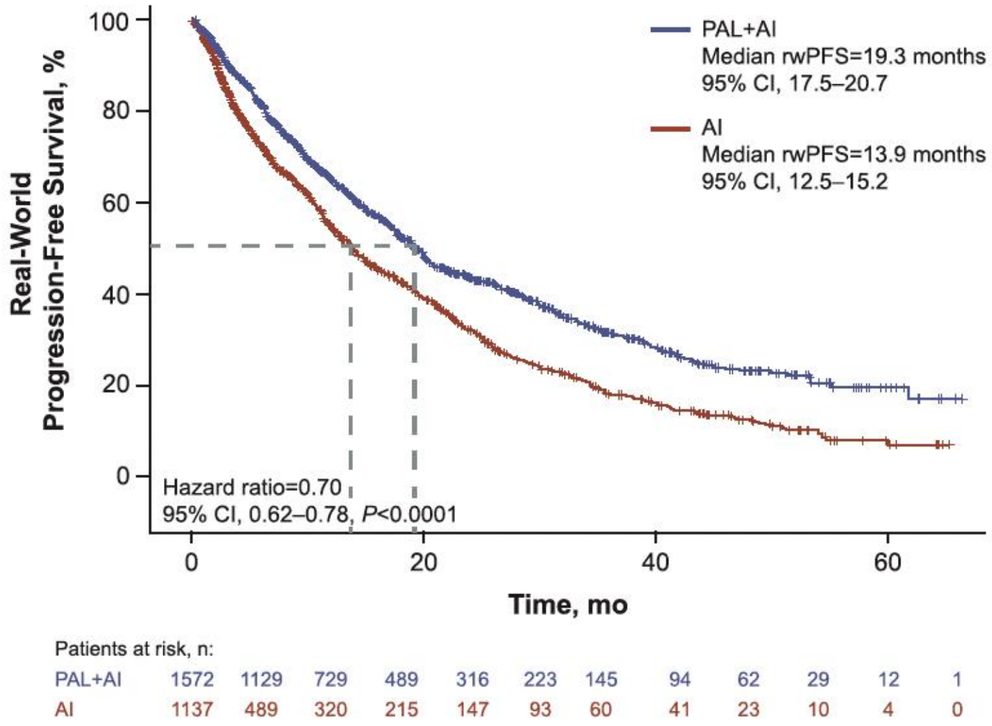
Real-world study of overall survival with palbociclib plus aromatase inhibitor in HR+/HER2− metastatic breast cancer

Hope S. Rugo[1✉], Adam Brufsky[2], Xianchen Liu[3], Benjamin Li[3], Lynn McRoy[3], Connie Chen[3], Rachel M. Layman[4], Massimo Cristofanilli[5], Mylin A. Torres[6], Giuseppe Curigliano[7], Richard S. Finn[8] and Angela DeMichele[9]

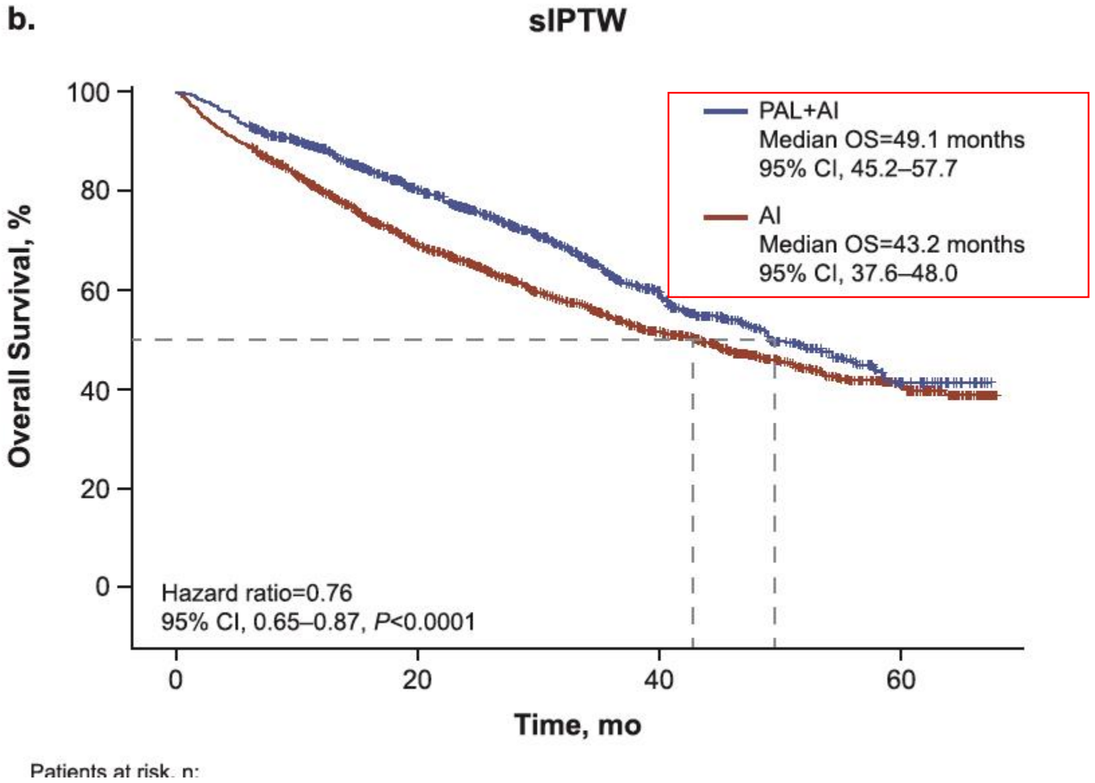
OS in the trial: 54 v 51 months

PFS

Stabilized inverse probability inerse weighting

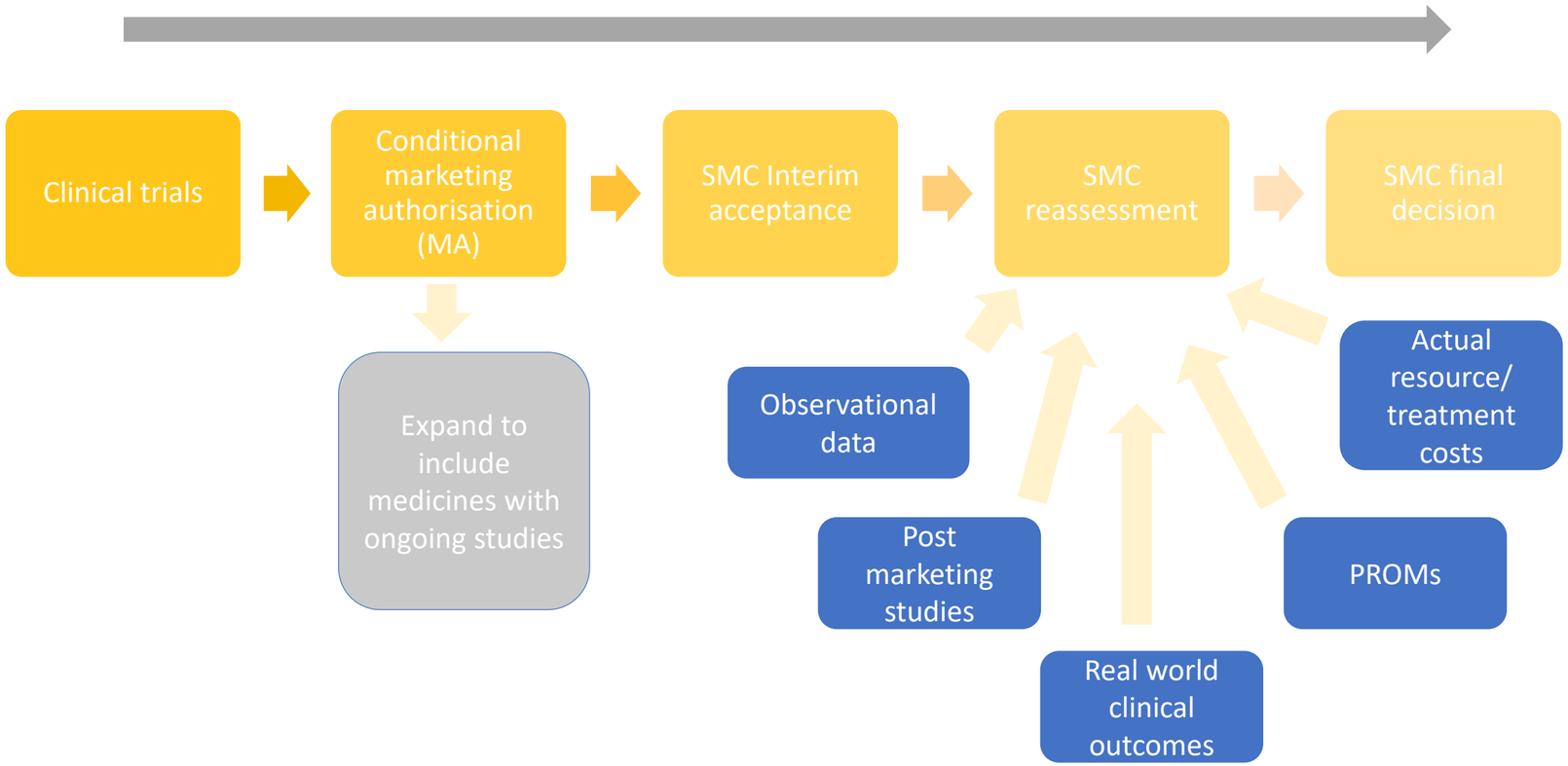


OS



Adaptive HTA……..

Continuum of evidence generation



Making Outcome-Based Payment a Reality in the NHS

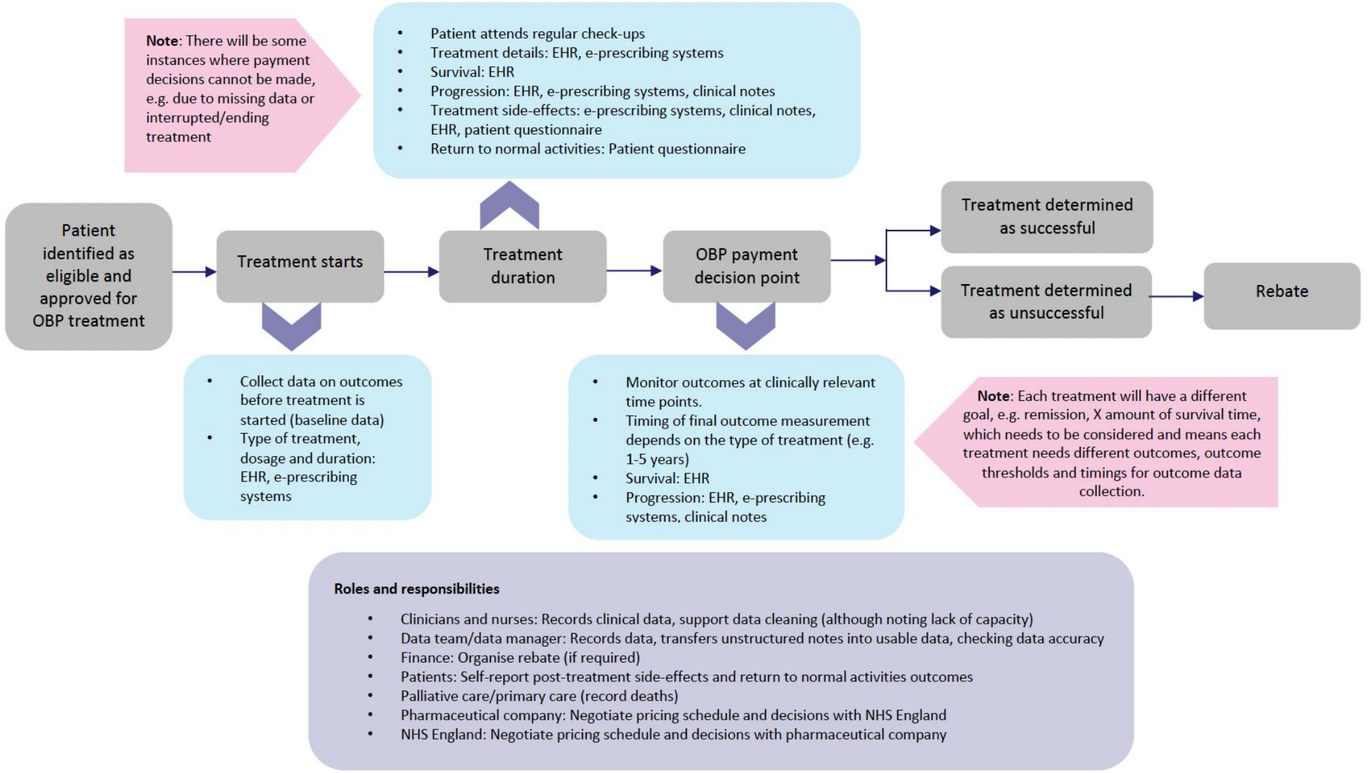
Phase 2: Practical Considerations

November 2021

Together we will beat cancer

Greater Manchester Health and Social Care Partnership

CANCER RESEARCH UK



Key: Grey box = Key points in the OBP pathway; Blue box = What types of data need to be collected and how; Pink box = Points to consider for data collection; Purple box = Roles and responsibilities

Figure 3 Flow diagram of an OBP scheme and the requirements at each stage

Flatiron Health

- Established USA 2012 – tech start up
- Bought by Roche 2018
- Set up UK 2019 - Works with NICE
- HDR –UK – Health data research

Efficacy/ Effectiveness Gap

- Marginal benefits in surrogate markers in trial populations result in even less benefit in real world populations.
- This has dramatic effective on quality of life calculations
- Different populations: RW v ideal trial population
  - Efficacy less
  - Toxicity more - which affects utility values in QUALY calculations
- Therapeutic window narrower
- Does this matter – in terms of ‘ THE TRUTH’ about efficacy – maybe not.
- However, has significant effect on Value and ICER
- NICE HTA Innovations Lab and new funding 2024 from Voluntary Pricing Scheme for branded medicines for HTA assessment

Real World Data from Scotland

How should it be used?

Julie Clarke – Lead Pharmacist, Cancer Medicines Outcomes Programme

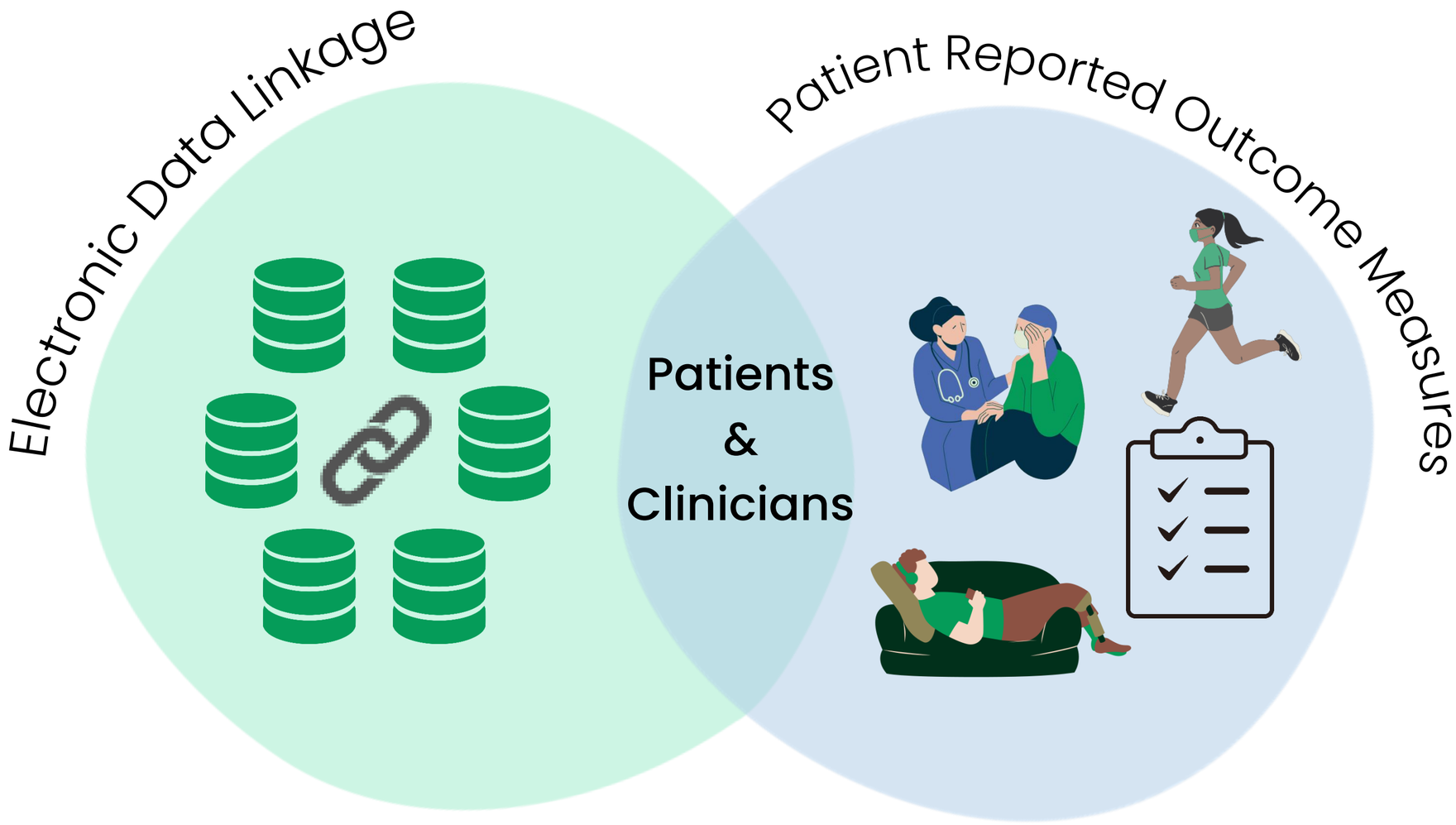
March 2024

Overview

- Vision
- Programme evolution
- RWE in use

Vision: To better understand the real life impact of cancer medicines on cancer patients in Scotland

CMOP
Cancer Medicines Outcomes Programme



Patient, Population & Policy

Evolution

- **Phase 1** (2016-2020)
  - GGC to WoS; Safe Haven; Prostate, melanoma, colorectal, gynaecological
- **Phase 2** (2020-2023)
  - WoS to National; Myeloma, immunotherapy
- **Transition** (2023-24)
  - National SACT data; test RWE with SMC, NCMAG, SCN

RWE for SMC / NCMAG

Aim: provide real world data to support SMC interim acceptance re-appraisal

- Who has received cemiplimab for advanced cutaneous squamous cell carcinoma?
- What are the baseline characteristics of this cohort?
- What are the outcomes of treatment?

RWE for Clinical decision making

- Early breast cancer SACT with SCN
- Immunotherapy refresh with exploratory adverse effects

2024 onwards

- What would you like to see?
- Best methods for engagement
- How to strengthen role of HTA
- Where should service provision and tumour testing fit in?
- Any new novel mechanisms for assessing cost effectiveness
- What should be the balance of priorities?
- Access to new medicines v delivery of service v uncertain data

THANK YOU

Julie.clarke2@ggc.scot.nhs.uk

@CMOProgramme

University of Strathclyde Glasgow

NHS Greater Glasgow and Clyde

CMOP Cancer Medicines Outcomes Programme

Scottish Government
Riaghaltas na h-Alba
gov.scot

Public Health Scotland

North Cancer Alliance

NHS West of Scotland Cancer Network

SCAN South East Scotland Cancer Network

NHS SCOTLAND

Working regionally to improve cancer services