EMA Cancer Medicines Forum (CMF) meeting with industry stakeholders on cancer treatment optimisation

Meeting report

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Disclaimer

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1. Background

The EMA in collaboration with the Cancer Medicines Forum (CMF) organised a workshop to enable industry support for cancer treatment optimisation.

The workshop aimed to foster dialogue on cancer treatment optimisation, focusing on industry support to the field both during the development phase and the post-marketing authorisation process, from innovation through clinical practice, and ways to facilitate effective stakeholder dialogue and communication.

Topics explored included optimisation strategies related to treatment dose and duration, reward mechanism for post-marketing studies, industry's role in supporting optimisation post-approval, and data and tissue sharing.

The presentations of the speakers and video recording of the workshop are published on EMA's website.

2. Welcome and introduction

Opening remarks

Francesco Pignatti, Scientific Adviser in Oncology at EMA, opened the workshop by highlighting that this event represents a natural evolution of the CMF since its establishment in 2022, with the Forum now expanding industry stakeholder engagement. He reaffirmed that treatment optimisation aims to resolve persistent uncertainties identified for oncology medicines, particularly where existing evidence does not sufficiently support optimal dose, duration, sequencing, or real-world therapeutic value.

The objective of the workshop was to strengthen understanding, foster collaboration, and secure a collective commitment to address these complex challenges moving forward.

Industry Perspective on Treatment Optimisation

Presentation by Michael Zaiac, Head of Medical Affairs Oncology, Daiichi-Sankyo Europe, Germany and Dominita Burcoveanu, Bayer jointly presented the industry perspective on treatment optimisation.

Dominita Burcoveanu emphasised that treatment optimisation is critical because dose, duration, and treatment sequence are often not fully understood at the time of Marketing Authorisation (MA). Many registration trials do not capture the complexity of real-world clinical practice. She stressed that optimisation requires input from clinical practice, patients, and payer systems to design pragmatic and adaptive clinical trials capable of assessing the real-world benefit–risk balance of medicines. Clear communication is particularly important when dose modifications are needed. She closed with a quotation from Winston Churchill: "Live today and fight tomorrow."

Michael Zaiac outlined the origins of the CMF, launched in 2022 as a non-advisory, multi-stakeholder forum including academia, HTAs, payers, and patient representatives. Its mission includes identifying priority optimisation questions, primarily in the post-marketing setting and to foster a collaborative research framework with a commitment to transparency and evidence-based recommendations. He also highlighted that the CMF has drafted a framework for when and how to run optimisation trials and discussed case examples which illustrated the benefits of de-escalation strategies both in terms of patients' outcomes and costs effectiveness. Rather than real-world comparisons, there is the need for Randomised Clinical Trials (RCTs) to generate robust optimisation evidence. This underscores the need for sustainable funding models, including payer engagement.

Michael Zaiac reviewed milestones in CMF development, including the December 2023 agreement on shared terminology and prioritisation logic, and the April 2024 workshop held under the Belgian Presidency of the European Council. These meetings confirmed EMA's commitment to integrating optimisation considerations into scientific advice and post-authorisation planning. He concluded with a second Churchill quotation from the Battle of El Alamein: 'Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning'.

Future Directions from Industry

Moving forward, Dominita Burcoveanu suggested that optimisation should become part of the expected lifecycle pre-approval, embedding optimisation recommendations into established mechanisms such as EMA Scientific Advice and HTA Joint Scientific Consultations. In the post-marketing setting, coordinated platform such as the CMF can support pragmatic multinational trials with funding mechanisms involving payers, public agencies and academic networks. This evolution of the CMF supports improved predictability for industry and better outcomes for patients.

3. Session 1: Finding the 'optimal dose' and duration– an ongoing challenge

Oncology Dose Optimisation: An Industry Perspective on Challenges & Opportunities

Presentation by Chunze Li, executive director and distinguished scientist, head of oncology clinical pharmacology at Genentech, with support from Paven Vajjah from AstraZeneca and Leslie Carter from AbbVie.

Chunze Li noted that traditional chemotherapy relied on Maximum Tolerated Dose (MTD) and Dose-Limiting Toxicity (DLT) as the basis for dose selection, assuming a strong correlation between higher dose, efficacy, and toxicity. With the advent of targeted therapies and monoclonal antibodies, this paradigm have shifted: higher doses do not necessarily produce greater efficacy and may instead introduce unnecessary safety risks. In many cases the Optimal Biological Dose (OBD) is more relevant, making DLT alone insufficient to define the Recommended Phase 2 Dose (RP2D). As a result, dose decision should be based on a comprehensive evaluation of both safety and efficacy. Chunze Li described a new, multidimensional framework for dose finding involving safety, efficacy, PK/PD biomarkers, long-term tolerability, and Patient-Reported Outcomes (PROs). Early-phase trials are increasing expected to serve multiple objectives, including MTD determination, patient population selection, proof of mechanism (PoM), Proof of Concept (PoC), and combination strategies, while navigating ethical constraints to minimize exposing patients to poorly tolerated or suboptimal doses. She highlighted several challenges: short observation windows, limited long-term tolerability data, lack of reliable biomarkers linked to efficacy, early endpoints that may not predict long-term outcomes such as PFS or OS, and the subjective elements inherent in benefit–risk decision-making.

Novel methods for dose optimisation include tailored strategies by molecule class, advanced modelling and simulation, and innovative study designs (e.g. BOIN, BOIN12, U-BOIN, DROID). Chunze Li illustrated these concepts using the development of polatuzumab vedotin (Polivy). She emphasised that dose optimisation is a continuous learning process across the full development lifecycle and should be integrated seamlessly into clinical development plan across the life cycle.

Looking ahead, she noted that circulating tumour DNA, real-world evidence, and AI/ML techniques could enable real-time dose adjustment and personalised dosing.

Should dose-finding be concluded pre- or post-approval?

Presentation by Olli Tenhunen, vice chair of the Oncology Working Party at EMA

Olli Tenhunen addressed whether dose finding should be completed pre- or post-authorisation. He traced the evolution of dose-finding studies from early chemotherapy development—where MTD was standard—through examples such as etoposide and oxaliplatin.

He recalled that EU legislation requires refusal of MA where quality, safety, or efficacy is insufficiently demonstrated (Articles 12 and 26 of Regulation (EC) 726/2004). Regulators assess the absolute benefit–risk of each medicine, not relative to alternatives.

Olli Tenhunen summarised key guidance: ICH E4 on dose-response information, EMA's anticancer guideline emphasising biologically active dose determination, and the FDA's 2024 guidance on oncology dose optimisation. He noted that MTD does not capture low-grade toxicities, cumulative burden, dose modifications, or PK/PD considerations. Dose optimisation must not impede efficient development, but it involves multifactorial assessment including tolerability, adherence, clinical benefit, subsequent therapies, QoL, and OS.

He also referenced an FDA analysis in the Journal of Clinical Oncology (Dosage optimization in drug development: An FDA Project Optimus analysis of post-marketing requirements issued to repair the cracks. | Journal of Clinical Oncology) showing a median six-year timeline to reach post-marketing dose optimisation across a set of oncology products. He also pointed to examples illustrating the complexity of dose-finding for certain medicines.

The forthcoming EU pharmaceutical legislation acknowledges the need for optimisation post-authorisation, enabling regulators to require additional studies where an applicant's proposed dosing regimen, while acceptable, could be improved.

Olli Tenhunen concluded that identifying dose-related uncertainties early and prospectively planning dose-optimisation strategies across the clinical development plan is essential.

4. Session 2: Reward Mechanisms for Post-Marketing Studies - Incentives for Optimisation

Balancing innovation and access: Insights from AIM's Fair Pricing model and its current and future applications

Presentation by Jocelijn Stokx, International Association of Mutual Benefit Societies

Jocelijn Stokx presented results from an AIM study assessing whether current market prices of new medicines reflect their underlying costs and therapeutic value. She highlighted that rising drug prices introduce increasing pressure on health systems, while evaluations such as the KCE study (Do innovative medicines against cancer always have a real value) show that many new cancer treatments provide limited survival benefit at the time of approval.

Using the AIM Fair Pricing Model, ten patented medicines across six European countries were analysed. The study found that fair prices were on average 53% lower than list prices and 34% lower than estimated net prices. Production costs accounted for a major share of prices, while R&D costs often represented only a small fraction. Innovation bonuses were generally low, reflecting limited added value for many products.

Estimated savings were substantial: €9.6 billion gross across the six participating countries and €27 billion annually at EU level. Belgium alone could save approximately €820 million per year. These findings confirm earlier studies showing large discrepancies between current prices and cost-based estimates.

Jocelijn Stokx emphasised that the AIM Fair Pricing Model provides a transparent, practical tool for negotiations—already used by Dutch insurers—and can be integrated with treatment optimisation strategies. Incentives such as innovation bonuses could be linked to companies conducting optimisation studies pre- or post-authorisation, while savings generated through fair pricing could help finance future optimisation research. Jocelijn Stokx noted that governments could redirect savings generated through fair pricing to finance treatment optimisation studies, creating a virtuous cycle of value generation.

Jocelijn Stokx concluded that current medicine prices are often not justified by underlying costs or therapeutic value. The AIM Fair Pricing Model offers a transparent, evidence-based approach that strengthens the negotiating position of health systems, supports financial sustainability and safeguards equitable access. Integrating fair pricing principles with treatment optimisation could further align incentives and promote better outcomes for patients across Europe.

Incentives to support post-marketing research

Presentation by Mike Akimov, Boehringer-Ingelheim

Mike Akimov presented on the growing role of real-world data (RWD) throughout the medicine lifecycle, from early clinical development to post-authorisation evaluation. He highlighted that RWD is increasingly used to complement clinical trials, inform regulatory submissions, and strengthen post-marketing assessments of safety and effectiveness.

From a regulatory perspective, several incentives encourage robust post-marketing evidence generation. Authorities may grant extended data or market exclusivity when companies complete agreed post-authorisation studies, such as paediatric investigations. In addition, accelerated and conditional approval pathways rely on early evidence, including surrogate endpoints and RWD, with the obligation to conduct confirmatory post-authorisation trials. Post-marketing RWE can also support requests for new indications, additional patient populations, or dosage refinements.

There are also important scientific and strategic drivers. Post-marketing RWD contributes to a more detailed characterisation of safety profiles, enhances risk-management activities, and aligns with regulatory expectations, as demonstrated by the evaluation of interstitial lung disease for early EGFR TKIs. RWE can help validate the external validity of trial results, support future lifecycle planning, and inform decisions on pricing, access, and clinical use. Engagement with clinicians and patient organisations during post-marketing research further strengthens stakeholder trust and fosters ongoing collaboration.

At the policy level, regulatory agencies such as EMA, FDA, and PMDA increasingly promote structured approaches to generating and analysing RWD. Investments in health-data infrastructures, registries, and multi-stakeholder consortia are also lowering barriers to producing high-quality RWE and enabling more consistent methodologies across jurisdictions.

Financial and market considerations additionally encourage post-marketing evidence generation. RWE can enhance submissions to health technology assessment bodies, support reimbursement decisions, and facilitate managed-entry agreements. Demonstrated real-world performance improves product differentiation and reinforces confidence among prescribers and healthcare institutions.

A relevant example is the RealGiDo study on afatinib in EGFR-mutated non-small cell lung cancer (Impact of afatinib dose modification on safety and effectiveness in patients with EGFR mutation-positive advanced NSCLC: Results from a global real-world study (RealGiDo) - ScienceDirect). This global

observational study, conducted across 13 countries and involving 228 patients, assessed the safety and effectiveness of afatinib in routine clinical practice. The findings showed that tolerability-guided dose reductions reduced the frequency and severity of adverse reactions without compromising treatment effectiveness. These real-world observations were consistent with clinical-trial outcomes and supported the value of dose individualisation. The case illustrates how high-quality RWE can substantiate clinical benefits, complement trial data, and inform regulatory and clinical decision making.

Incentives to support post-marketing research

Presentation by Francis Nissen, Kite/Gilead

Post-marketing studies allow for the collection of additional data on safety and effectiveness, enabling real-world insights. They are defined as studies conducted after a medicine has been granted MA to monitor its safety, efficacy/effectiveness, and long-term effects in a larger, more diverse real-world population. Routinely performed post-authorisation studies aim to address regulatory needs regarding safety and/or effectiveness; support local reimbursement requirements and maintenance; validate clinical trial data in the real-world setting, generate critical evidence to support value differentiation, assess treatment sequence (including adherence, prescribing patterns, treatment switching), generate evidence in specific sub-populations, establish head-to-head comparison, and support label expansion.

Francis Nissen highlighted that post-marketing research is recognised by key decision-makers to improve patient care. It is considered by regulators for regulatory decisions, informing and accelerating new drug approvals, supporting robust post-marketing confirmation through safety monitoring and surveillance studies, and facilitating post-marketing changes such as label updates, population expansions, or new indications. It informs reimbursement decisions taken by payers, providing comparative evidence to contextualize single-arm or uncontrolled trials and generating real-world post-launch data to inform reassessment and potential price re-evaluation. it supports clinical decisions taken by medical societies and physicians as it provides deeper insights into treatment effectiveness and safety to guide clinical decisions, understanding on long-term patient outcomes, and identifying unmet needs that can shape future research.

As illustrated by Francis Nissen's example of CAR-T therapies, adaptive regulation involves continuously updating regulatory requirements based on emerging evidence and real-world experience. In the cell and gene therapy field, the 15-year long-term follow-up requirement for integrating vectors was originally introduced as a precautionary measure due to concerns about insertional oncogenesis.

Innovative reward mechanism

Presentation by Sahar van Waalwijk van Doorn-Khosrovani, Pharmacist Medicine & Society, CZ, National Funder's Committee for Evaluation of Specialised Medicines and Companion Diagnostics (CieB,AG), Prime-Rose Consortium, Leiden University Medical Centre.

Sahar van Waalwijk van Doorn-Khosrovani started her presentation with a recent publication titled determining the optimal use of approved products in Oncology published in the Lancet Oncology: Determining the optimal use of approved drugs in oncology - The Lancet Oncology. Payers are often asked to support treatment optimisation to reduce costs of medicines. In the Netherlands, the study drug can be reimbursed in most treatment optimisation studies. The article showcases different scenarios of treatment optimisation, such as decreasing doses or duration of treatment to lower unnecessary costs or improve patients' quality of life. It also proposes strategies to prioritise treatment optimisation studies, with the highest priority given to improving efficacy, reducing side-effects and improving quality of life. Addressing financial toxicity is also an important factor, as it can contribute to improving health outcomes

for other patients by freeing up healthcare budgets for them. Sahar van Waalwijk van Doorn-Khosrovani provided examples in resected Stage III or IV melanoma, citing the EORTC 1325 / KEYNOTE-054 and CheckMate-238 studies, which established a new standard of care years ago: one year of adjuvant therapy with immune checkpoint inhibitors. However, it remains unclear why one year is needed or for whom. Based on the Dutch health claims data from 2020-2025, there has been a continuous decline in the number of patients receiving adjuvant therapy in line with the label. This could be explained by a lack of trust in these therapies due to concerns about overtreatment, long-term clinical and financial toxicity, as well as overall survival data that were either not reported or negative. Fortunately, two dose optimisation studies provided results to support decision-making. A private-public partnership (National Cancer Institute and Merck Sharp and Dohme) funded SWOG S1808 treatment optimisation study that divided the dose of adjuvant therapies into three neoadjuvant doses and 15 adjuvant doses. Another dose optimisation study was the NADINA trial in resectable stage III melanoma. This investigator initiated clinical trial, financed by Bristol Myers Squibb, studied the effect of two cycles of neoadjuvant ipilimumab plus nivolumab followed by surgery. This resulted in a high percentage (59.0%) of patients achieving a major pathological response, in whom the 12 cycles of adjuvant therapy could be omitted. Both trials showed long-term advantage compared with the original adjuvant-only treatment schedule. In the Netherlands, these optimised regimens are increasingly being used.

Overall, post-marketing dose-optimisation studies could lead to a competitive advantage for companies, making their drug the treatment of choice, as resource-saving strategies encouraged by hospitals and payers may benefit society, and improved efficacy and safety profiles makes clinicians more confident in their treatment decisions.

5. Session 3: Collaborations and Partnerships — Industry's Role in Supporting Optimisation Post-Approval

Industry support for pragmatic trials and real-world evidence studies

Presentation by Nafsika Kronidou, Roche, EFPIA Pragmatic Trials sub-group lead, with support from Liz Poole, Jazz Pharmaceuticals

The foundational work of Nafsika Kronidou 's presentation is based on the EFPIA position paper (June 2023) on randomised pragmatic trials to generate high-quality real-world evidence for regulatory decisions and case studies which were used to contextualize the opportunities and potential barriers.

The traditional randomized clinical trials have become complex, adding burden to patients, sites and sponsors. In oncology, only a limited number of patients participate in clinical trials and often the evidence from traditional pivotal trials generated under highly controlled conditions do not reflect clinical practice. For this reason, there is a need to consider different study designs such as trials with pragmatic elements.

Compared to traditional trials, trials with pragmatic elements can be more patient-centric and reduce burden on participants and investigators e.g., fewer visits, fit-for-purpose data collection; focus on patient-relevant outcomes (e.g., mortality and PROs); generate evidence closer to clinical practice; increase external validity; and leverage real-world data sources e.g., EHRs, registries, and data from digital health technologies. These features could enable broader patient participation in clinical trials

The PRECIS-2 tool (please see slide 8 of the presentation) was developed to help design trials with pragmatic elements. This tool considers the following 9 elements: eligibility, recruitment, setting, organisation, flexibility/delivery, flexibility/adherence, follow-up, primary outcome and primary analysis.

The degree of pragmatism for each element will depend on the scientific context and available information.

Following initial approval, additional evidence is often required, for example indifferent patient groups e.g. older adults or unstudied co-morbidities etc. As understanding of the molecule grows post-authorisation, confidence in introducing pragmatic elements also increases.

Nafsika Kronidou provided 2 hypothetical case studies in Oncology which focus on treatment optimisation and implementing pragmatic elements. The 1st example was to address evidence gaps in a special patient group when the pivotal trial leading to approval did not enroll sufficient patients in that group (e.g. older adults). Assuming that there is no evidence or biological rationale for increased risk in this patient population, pragmatic elements such as selective safety data collection, reduced frequency of assessments and focus on severe AE, tolerability and PRO could be introduced. In the 2nd example, Nafsika Kronidou explored the use of EHR and death registries to capture mortality outcomes in the maintenance part of a pivotal study

In both case studies, the introduction of pragmatic elements may carry actual or perceived risks e.g. on the trial outcome, methodological or on the acceptability of these elements/ data by regulators (see slide 13).

There is very limited experience in leveraging evidence from randomized pragmatic trials for regulatory decisions. For this reason, Nafsika Kronidou concluded that there is a need to build awareness, expertise, and confidence on this study concept. She highlighted the importance of fostering collaboration and co-designing solutions to advance the use of pragmatic approaches. This includes establishing robust methodological approaches and standards, and ensuring the involvement of key stakeholders such as patients, regulators, real-world data custodians, academic groups, and industry representatives. Sharing learnings from specific case studies and addressing existing gaps was highlighted as a priority, with workshops, conferences and publications serving as key platforms for disseminating experiences. Regulators were encouraged to share their collective experience in evaluating such data to enhance transparency and consistency. The discussion also underscored the need for global regulatory alignment, aiming to drive consistency in interpretation across EU Member States and promote harmonisation of regulatory approaches internationally. Finally, she stressed the importance of mindset shifts within the community, advocating for greater adoption risk-proportionality principles and tangible examples to move away from the rigid "more data is better" paradigm.

Collaborative models with academia and research institutions

Presentation by Denis Lacombe, Chief Executive Officer, EORTC

He explained that the objective of the Cancer Medicines Forum when initially set up was to increase the uptake of academic clinical trials to support regulatory decision and label update.

Denis Lacombe highlighted opportunities for collaboration between commercial and non-commercial sectors in clinical research, emphasising the diversity of trial types that could benefit from shared efforts. Denis Lacombe's presentation focused on models of international, multi-centric clinical trials, highlighting the value of prospective datasets built on robust methodologies to advance treatment-related knowledge and drive changes in clinical practice.

He discussed the reasons for collaboration from both industry and academic perspectives. For industry, partnerships offer access to specialised networks and methodological expertise, opportunities to go beyond primary indications, the ability to conduct investigator-initiated trials not managed by CROs, and the chance to maintain scientific dialogue with learned societies. Academia benefits from access to pipelines of new agents, contributing to therapeutic progress, addressing gaps in scientific strategies, and pursuing research in specific clinical situations such as rare cancers and older patient populations.

There are clinical scenarios that are particularly conducive to partnerships, including label extensions to new tumor types not primarily targeted by industry, earlier lines of treatment within the same indication, and recruitment through specialised networks such as neuro-oncology or sarcoma. Access to specific patient populations, optimisation in subgroups through biomarker research, and cross-cutting expertise in areas like multi-tumor approaches and radioligands were also highlighted. Certain trial designs were noted as especially relevant for collaboration, including complex basket and umbrella trials, studies incorporating quality-of-life and patient-reported outcomes, registry-based trials such as Trials Within Cohorts, pragmatic clinical trials focused on methodological and implementation research, and multidisciplinary trials involving radiotherapy or peri-operative interventions.

The EORTC's capabilities were presented as a strong foundation for such collaborations. With a long-standing history of successful drug approvals and registrational studies, EORTC offers integrated services encompassing protocol development, site activation, data management, monitoring, analysis, data control, and reporting. Its peer review process ensures methodological rigor and transparency, increasing the likelihood of success for proposed programs. EORTC combines flexibility with efficiency, adapting to evolving partner needs while maintaining aggressive timelines, achieving first patient first visit within four to six months of protocol finalisation, and offering competitive cost structures. Its global reach spans Europe, the United States, and Asia-Pacific, supported by multidisciplinary expertise in radiation oncology, rare cancers, elderly populations, and quality-of-life research. Equipped with tailored infrastructures for complex trials, EORTC provides access to diverse tumor types and rare cancers, enabling integral solutions based on translational science.

Denis Lacombe presented the case example of DE-ESCALATE in prostate cancer (EORTC GUCG 2238 De-escalate: A pragmatic trial to revisit intermittent androgen-deprivation therapy in metastatic hormone-naïve prostate cancer in the era of new AR pathway inhibitors. | Journal of Clinical Oncology), designed with patients and supported by a grant from the European Commission, which aims to have intermittent androgen deprivation treatments when patients have achieved a significant PSA decline as the new SOC, with the view to improve patients' quality of life.

Overall, the rethinking of partnerships between commercial and independent sectors can optimise stakeholder roles in development and access, create opportunities for treatments' optimisation and methodological innovation, and leverage independent research to advance therapeutic progress beyond primary development agendas. Such collaborations can address patient populations often excluded from regulatory trials, including older adults and those with rare cancers, and support multidisciplinary and combination approaches. Ultimately, these efforts contribute to a sustainable economic model for cancer research, development, and access.

6. Session 4: Data Sharing and Tissue Banks — Moving Forward

Opportunities in sharing molecular clinical data

Presentation by Pr. Jonas Bergh, Dept of Oncology-pathology, Karolinska Institutet and Karolinska Comprehensice Cancer Center, Karolinska University Hospital, Sweden

Jonas highlighted the evolving landscape of cancer drug development and the shifting roles of key stakeholders. Over recent decades, innovations and early development efforts, by different stake holders, in the early phases of course including research groups at universities. The pharmaceutical industries have been instrumental in running clinical studies aiming at approvals of new drugs/indications. Altogether during the last two decades that has resulted in exponential increase the in the number of new

cancer drugs, most of them being so called targeted drugs and immune system activators. access to novel cancer medicines. These advances have been driven by a deeper molecular understanding some of mechanisms in normal cellular growth control and alterations/factors involved in malignant transformation. Based on a better understanding of these processes that have resulted in better opportunities for rational drug design, ideally resulting in improved responses and patient outcomes and, in some cases, reduced cancer-spe mortality. However, a noticeable decline in academic involvement in recent years is observed. The lack of academic influence could lead to less fine-tuned study designs not investigating the individually fine-tuned molecular mechanisms for the anti-tumoural effects/, and which patients are at risk to develop side effects.

Academic-led studies, which historically contributed significantly to translational science, have diminished, raising questions about whether the depth of mechanistic research is being compromised, including less optimal clinical study designs, resulting in that too many patients are potentially treated too long. (e.g. patients with pathological complete response may not need to also receive the tested drug in the adjuvant setting, because some patients may have been cured already in the neoadjuvant phase- "A third arm" in the design could likely have handled this question. Some industry representatives view this trend positively, citing efficiency gains, while others worry that

The EMA conditional marketing authorisation process allows medicines addressing unmet medical needs to be approved based on less comprehensive clinical data when the immediate availability of the drug outweighs the risks associated with incomplete evidence. While this approach accelerates marketing authorisation, it raises critical questions: should the approval process merely satisfy regulatory requirements, or should it also aim to deepen understanding of tumour biology to optimise the benefit-risk balance? Jonas discussed how additional data should be obtained and emphasised that patients, as owners of their biological materials, should play a more active role in research. Furthermore, academia and payers were identified as essential contributors to these processes, alongside the Market Authorisation Holders who currently dominate compliance with EMA and FDA requirements.

The conversation highlighted several scientific and clinical challenges. For example, pathological complete response (pCR) is recognised as a strong prognostic factor in breast cancer following neoadjuvant therapy, but uncertainties remain regarding the need for additional therapies post-pCR, especially given the potential for serious side effects and economic implications. Advanced strategies such as multi-omics profiling and liquid biopsies were discussed as promising tools to capture interpatient heterogeneity in treatment response and toxicity. However, these approaches are often underutilised in registration trials, potentially missing opportunities to refine benefit-risk assessments. Questions persist about whether liquid biopsies accurately reflect the complexity of tumour and stromal compartments, and participants agreed that integrating multi-omics and SNP profiling on both tissue and circulating samples is critical.

The role of academia in these advanced analyses was emphasised, as academic institutions are well positioned to explore these scientific avenues. Yet, they are rarely involved in building registration dossiers, prompting concerns about whether this trend serves the best interests of patients and society. Jonas also stressed the importance of using appropriate biopsy material, particularly metastatic rather than primary samples, and leveraging biobanked resources to correlate molecular findings with therapeutic outcomes. Sequential biopsies and liquid biopsies were considered valuable for tracking tumour evolution, which is known to involve clonal changes and new mutations during progression. Countries with comprehensive population-based registries, such as those in the Nordic region, the Netherlands, and the UK, were identified as ideal settings for long-term studies that capture relapses, comorbidities, side effects, and causes of death.

Several case examples were referenced, including multi-omic profiling studies in HER2-positive breast cancer and trials conducted by the Scandinavian Breast Group (Interplay between copy number alterations and immune profiles in the early breast cancer Scandinavian Breast Group 2004-1 randomized

phase II trial: results from a feasibility study | npj Breast Cancer), as well as recent systematic reviews on genomic analyses of archival breast cancer tissue (Systematic review and feasibility study on pre-analytical factors and genomic analyses on archival formalin-fixed paraffin-embedded breast cancer tissue). These examples underscore the potential of advanced molecular approaches to inform predictive biomarkers and improve clinical decision-making.

Overall, there is an urgent need to reintegrate academia into early-phase and translational research, broaden stakeholder involvement to include patients and payers, and prioritise advanced molecular strategies to capture heterogeneity, and to better understand the differences in outcomes using modern molecular fingerprinting strategies (mutational patterns, SNP patterns, proteomics, immune cells and signatures).

Finally, tissue biopsies, plasma, and whole blood derived from the patients at study inclusion and longitudinal samples during study period seem not always to be used by the MAH. To leave such valuable human materials unused, and not being accessible to others than the MAH, cannot be interest of the patients of the patients having donated it, and will also be a disservice to other patients and societies.

Collaborative frameworks and innovative trial designs are essential to ensure that cancer drug development continues to serve both patients and society effectively.

Advancing Cancer Research Through Shared Data & Samples

Presentation by Pr. Christine Desmedt, LKI - KU Leuven Cancer Institute, Belgium

Christine Desmedt started her presentation by highlighting that 53 academic clinicians, researchers, and patient advocates worked on a global initiative to advance cancer research through shared data & samples (Enhancing Clinical Cancer Research Through Sharing of Data and Biospecimens | Research, Methods, Statistics | JAMA Oncology | JAMA Network).

She emphasised that molecular analyses of biospecimens collected from study participants are essential for identifying predictive biomarkers that can tailor treatments to specific subsets of patients most likely to benefit. Sharing data and biospecimens from clinical trials was recognised as a cornerstone for enabling personalised, patient-centric cancer therapy and accelerating the development of new treatments.

There is an increasing role of the pharmaceutical industry in cancer research, citing an analysis of more than 23,000 cancer trials registered on ClinicalTrials.gov (Patient Enrollment to Industry-Sponsored Versus Federally-Sponsored Cancer Clinical Trials | Journal of Clinical Oncology). Enrolment ratios (industry-sponsored studies versus federally sponsored trials) in cancer clinical trials have grown significantly in the United States, rising from 4.8 between 2008 and 2012 to 9.6 between 2018 and 2022. While this trend reflects industry's growing influence, it also underscores the need for robust data-sharing practices to ensure transparency and scientific progress.

The group examined existing policies and practices around data sharing. The National Institutes of Health has required data-sharing plans for new grants since 2003, and the International Committee on Medical Journal Editors has issued clear statements supporting data sharing. The EMA publishes clinical reports detailing trial methods and results, yet practical implementation remains limited and challenging. A recent review of 91 registration oncology trials from 16 pharmaceutical companies revealed that individual participant data (IPD) sharing occurs through platforms such as Vivli, ClinicalStudyDataRequest.com, and Yale University Open Data Access, as well as proprietary systems (Heterogeneity and Utility of Pharmaceutical Company Sharing of Individual-Participant Data Packages). While IPD packages were obtained for 77 percent of trials, the median time to data provision was 123

days, and significant heterogeneity was observed in the completeness of shared data, including redactions of outcome data, assessment details, and adjustment variables, as well as frequent absence of full study reports.

The collection of biospecimens was another critical point. Among 29 registration trials leading to breast cancer drug approvals between 2017 and 2024, participants were increasingly asked to provide tissue and body fluid samples, often at multiple time points (Enhancing Clinical Cancer Research Through Sharing of Data and Biospecimens | Research, Methods, Statistics | JAMA Oncology | JAMA Network). Despite this, translational research publications based on these samples remain scarce or delayed. Predictive biomarker analyses in registration trials are limited; while new therapies often receive broad drug labels based on statistically significant improvements in protocol-defined endpoints, efficacy is frequently restricted to specific patient subsets. Of the 29 trials reviewed, only 20 published biomarker studies, most of which were exploratory, and none resulted in changes to drug indications. Successful examples of biomarker-driven insights have emerged outside registration trials, such as HER2 status in patients treated with CDK4/6 inhibitors in PALOMA trials and body mass index correlations in HER2-positive breast cancer across multiple studies, as well as adaptive platform trials like I-SPY2 and collaborative efforts such as PALLAS.

Christine Desmedt highlighted several critical areas for improvement. Trial design and conduct should incorporate co-leadership structures between industry and academia to ensure comprehensive data collection, prospective biomarker testing beyond standard markers, planned analyses for toxicity, and validation in real-world settings. Patients play a pivotal role by consenting to donate data and samples for correlative science aimed at developing more tailored treatments. Patients often assume their care teams and academic partners are fully engaged in trial design and subsequent analyses, underscoring the need for greater public and patient involvement and explicit communication in informed consent forms about the intended use of clinical and biomarker data.

Despite existing mechanisms, pharmaceutical companies typically retain full control over which projects are approved, which data are released, and when analyses occur. She advocated for making data sharing a regulatory requirement, with plans developed proactively at the time of study design to address patient consent, data formats, legal and ethical considerations, platforms, and timelines. Standardisation of IPD packages is essential to enable post-approval meta-analyses. Similarly, biospecimen custodianship plans should be established early, and destruction of samples should be avoided. Standardisation of biomarker assays and interpretation was identified as a priority, along with rapid sharing of biological data to prevent duplication and resource waste. Platforms such as cBioPortal were suggested for disseminating biomarker results, supported by robust documentation and harmonisation.

The benefits of broader sharing of data and samples were widely acknowledged. Such practices boost patient engagement, build public trust through transparency, drive innovation by enabling new discoveries, and improve scientific credibility. They also influence policy, optimise drug use by focusing on subpopulations with meaningful clinical benefit, accelerate approvals and reimbursement, and advance science through academic collaboration that identifies novel drug targets. Ethical and socially responsible approaches to data and sample sharing were noted as appealing to investors and essential for sustaining progress in cancer research.

In conclusion, there is a need for a cultural and structural shift toward collaborative frameworks that prioritise transparency, patient involvement, and academic engagement. By standardising data and biospecimen sharing practices and embedding these principles into trial design and regulatory requirements, stakeholders can collectively accelerate the development of personalised cancer therapies and improve outcomes for patients worldwide.

7. Panel Discussion: Opportunities Ahead

Industry representatives: Francis Nissen (Kite-Gilead); Pavan Vajjah (AstraZeneca); Liz Poole (Jazz Pharmaceuticals); Marieke Schoonen (Amgen, EUCOPE)
ESMO representative: Dirk Arnold
EHA representative: Tarec Christopher El Galaly
EORTC: Denis Lacombe
Regulator: Pierre Demolis, oncology working party chair, EMA

Regulatory considerations: Pierre Demolis opened the panel discussion by emphasising that companies seeking marketing authorisation must generate sufficient data to demonstrate a positive benefit–risk balance. Historically, early cancer treatments relied on highly toxic chemotherapy agents, with regulatory focus placed primarily on proving efficacy and accepting significant toxicity due to the life-threatening nature of the disease. Today, with improved survival prospects in many cases, this paradigm has evolved. Regulators now expect optimisation of treatment strategies from the earliest stages of drug development. For example, in multiple myeloma, clinical trials often fail to include the population most in need (i.e. older adults) and include younger and fitter patients to guarantee a better successful clinical trial outcome. There is an urgent need to evolve for the benefit of patients as well as to address these high healthcare costs that governments have to carry. To change these long-standing practices, incentives could be introduced to encourage companies to develop medicines appropriately, ensuring that all relevant information is available at the time of authorisation. Decision-making occurs at multiple levels: investors, regulatory agencies, the European Commission, governments, and payers making coordinated support essential. Ultimately, strong leadership and collaboration are needed to achieve better treatment outcomes for patients in this global environment.

Pavan Vajjah emphasised that dose optimization may hold different meanings for different stakeholders. He referenced the FDA's Project OPTIMUS, which encourages companies to conduct randomized trials aimed at optimizing treatment regimens, a process that has already begun. He noted that optimisation should start with better data collection during the first registration of indications. Additionally, he stressed the need for treatment optimisation in older adults, an area that remains largely unaddressed.

Dirk Arnold commended the organisation of the workshop, highlighting the importance of discussions on treatment optimisation in oncology. A critical aspect, he noted, is treatment de-escalation, shortening treatment duration or reducing treatment intensity where appropriate. He reiterated ESMO's commitment to the healthcare environment and its global collaboration efforts, including the use of the Magnitude of Clinical Benefit Scale to assess treatments value. Methodological considerations with regards to non-inferiority trials could be further discussed to ensure that data generated would enable aligned clinical and regulatory decisions.

Liz Poole argued that "more" is not always better when it comes to dosing. She also pointed out the challenges of implementing changes post-marketing and suggested that regulators could require companies to collect real-world data once treatments are used in broader patient populations. Furthermore, she proposed leveraging lessons learned from paediatric cancer treatment as a potential path forward.

Marieke Schoonen emphasised the many opportunities for leveraging real-world data, for example, to improve understanding of disease characteristics, patient profiles, and expected side effects. She also highlighted the significant potential of novel biomarkers. Building trust and ensuring transparency are essential to advance treatment optimisation. Smaller hospital registries could be analysed more effectively, and the upcoming European Health Data Space represents a major opportunity in this regard.

Tarec Christopher El Galaly discussed the challenges of using real-world data throughout the cancer medicine development lifecycle, emphasising that confounding factors often make it difficult to use such data for regulatory decisions. In haematology, cancer treatments have been highly successful, with life expectancy approaching normal levels. However, as a clinician, he noted the limitations of current labelling, which recommends discontinuing treatment only when major side effects occur despite evidence that patients might benefit from treatment breaks. Robust clinical data are needed to support any changes to labelling. He stressed the importance of collaboration and alignment of objectives needed among academia, regulators, and industry to optimise knowledge, ensure data quality, address methodological challenges for the benefit of patients.

Francis Nissen mentioned that it is important to gather all perspectives to understand where the priorities lie. The right incentives need to be in place to move things forward.

Denis Lacombe explained that the EORTC launched its treatment optimisation initiative in oncology in 2013 and spent five years convincing the European Parliament of its relevance and critical importance. A manifesto was published in 2018, followed by the creation of the Cancer Medicines Forum in 2022. Now is the time to re-engineer, deliver, and implement prospective treatment optimisation to improve healthcare outcomes. Academia has a key role to play in addressing societal questions and ensuring continuous learning within healthcare systems. Research should also focus on healthcare delivery itself.

Christian Gisselbrecht raised concerns about the challenges of integrating clinical and biological data across studies. Clinicians might not have the biological data, and there is a need for regulatory and ethical oversight to facilitate data sharing and adapt to technological changes.

Philip Josephson, CHMP member Sweden, discussed the regulatory and methodological challenges in designing and interpreting de-escalation or de-intensification studies, including establishing scientific equivalence, acceptable uncertainty, and appropriate endpoints for labelling changes. There might be a need for guidance on when equivalence is established considering the need for high sample size and duration, which endpoints need to be similar. Stakeholders input on these aspects would be helpful in this regard.

With regards to patient involvement and perspectives in research, the participants emphasised the importance of including patient perspectives in research, drafting patient informed consent, regulatory decisions, and trial design, highlighting the value of patient organisations as active collaborators. An example was provided regarding the potential benefits of monitoring blood concentrations to minimise toxicities and side effects of everolimus. This approach is already used in transplant patients to prevent graft-versus-host disease and could similarly be applied to cancer patients, who often discontinue treatment due to adverse effects.

8. Conclusion

The workshop highlighted the maturing role of the Cancer Medicines Forum as a collaborative platform to address treatment and dose optimisation challenges in oncology. Participants converged on several themes:

- Optimisation must begin early in development and continue post-authorisation.
- Industry, regulators, HTAs, payers, and academia must collaborate to generate robust evidence.
- Sustainable funding and pragmatic multinational trial platforms are needed.
- Novel study designs, biomarkers, pragmatic trial, and modelling/simulation will be central to future optimisation.

The CMF will continue to advance coordinated, evidence-driven approaches to ensure that oncology medicines are used at the right dose, for the right duration, in the right sequence ultimately improving outcomes for patients across Europe.

The workshop confirmed that treatment optimisation in oncology must be addressed as a continuous, lifecycle process, beginning early in development and extending post-authorisation. Achieving meaningful optimisation requires coordinated action by regulators, industry, academia, HTAs, payers, and patients, supported by robust evidence generation, sustainable incentives, and transparent collaboration.

The CMF will focus on translating shared principles into implementation through targeted, outcome-oriented actions.