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Session 5: Opportunities and Challenges for Reporting Findings from Clinical Cancer Research Back to Participants

Pharmaceuticals Perspective

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Disclosure

No conflicts of interest to disclose

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Why Informing Patients on Study Results Matters

- Respects participants' contributions
- Builds trust and transparency
- Meets ethical and regulatory standards
- Improves public understanding of research
- Strengthen relationship to advocacy groups
- Supports patient-centered care
- Support future research

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Transparency Challenges[1-8]

- 20–50% of trials remain unpublished within 2–5 years
- 1/3 show discrepancies in primary outcomes between registry and publication
- Results often delayed or incomplete
- Patients infrequently receive updates directly

1. Lancet 2014; 383: 257–66
2. PLoS Med 2022; 19: e1003980
3. Facets 2023; 8: 1–10
4. BMJ 2016; 352: i637
5. BMJ Open 2023; 13: e076264
6. JAMA 2004; 291: 2457–65
7. JAMA New Open 2019; 2: e197242
8. J Clin Epidemiol 2017; 91: 87–94

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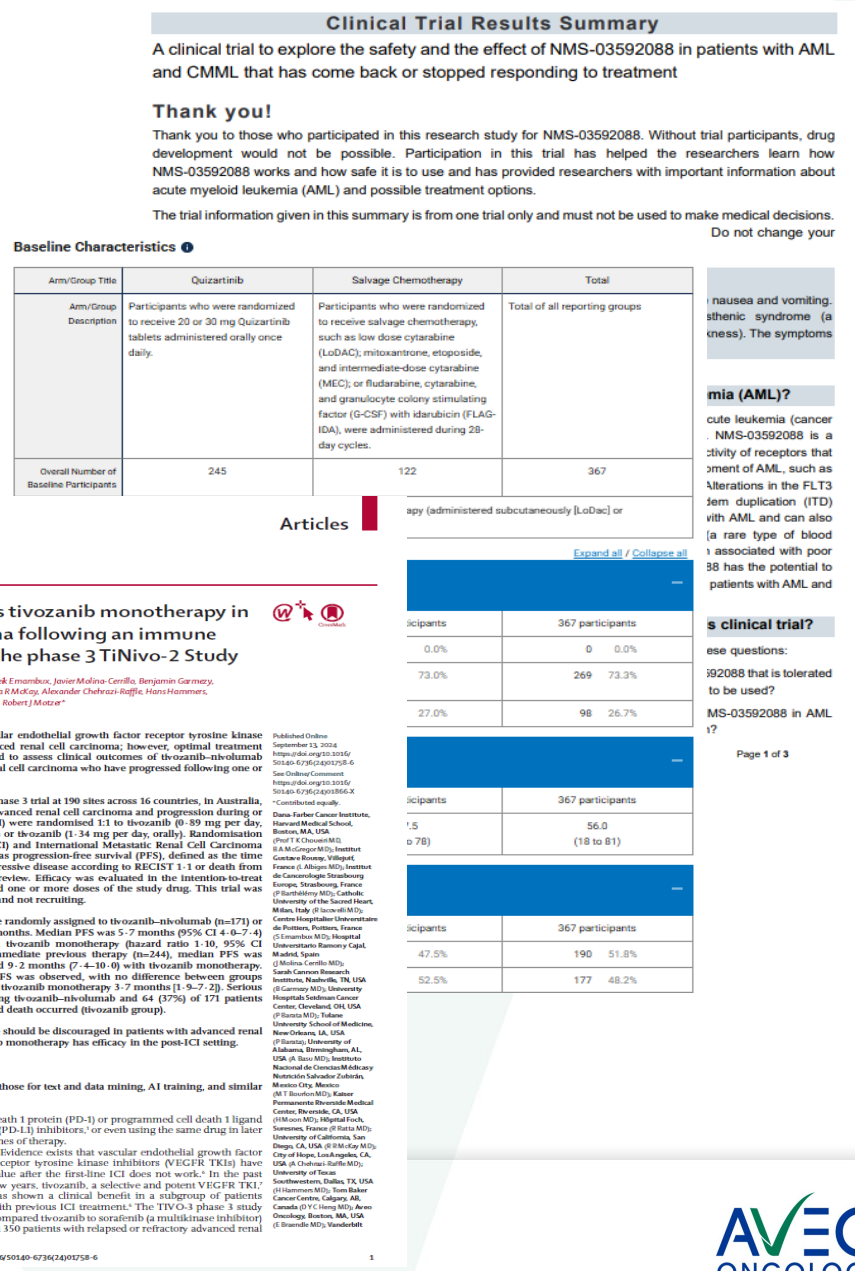
Different Forms of Reporting

- Plain Language Summary (PLS / LS)
- Posting results on trial registries
- Peer-reviewed publications
- Direct communication to patients
- Accessible online platforms

Posting clinical trial results registries does not preclude to publish in peer-reviewed publications and to provide a PLS/LS[1].



Clinical Trial Results Summary

A clinical trial to explore the safety and the effect of NMS-03592088 in patients with AML and CMML that has come back or stopped responding to treatment

Thank you!

Thank you to those who participated in this research study for NMS-03592088. Without trial participants, drug development would not be possible. Participation in this trial has helped the researchers learn how NMS-03592088 works and how safe it is to use and has provided researchers with important information about acute myeloid leukemia (AML) and possible treatment options.

The trial information given in this summary is from one trial only and must not be used to make medical decisions. Do not change your

Baseline Characteristics

Arm/Group Title	Quizartinib	Salvage Chemotherapy	Total
Arm/Group Description	Participants who were randomized to receive 20 or 30 mg Quizartinib tablets administered orally once daily.	Participants who were randomized to receive salvage chemotherapy, such as low dose cytarabine (LoDAC); mitoxantrone, etoposide, and intermediate-dose cytarabine (MEC); or fludarabine, cytarabine, and granulocyte colony stimulating factor (G-CSF) with idarubicin (FLAG-IDA), were administered during 28-day cycles.	Total of all reporting groups
Overall Number of Baseline Participants	245	122	367

Articles

Tivozanib plus nivolumab versus tivozanib monotherapy in patients with renal cell carcinoma following an immune checkpoint inhibitor: results of the phase 3 TiNivo-2 Study

Summary

Introduction

1. Ann Intern Med. 2023 Mar;176(3):eL220490. doi: 10.7326/L22-0490)

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US Regulations & Policies

- Results must be posted on ClinicalTrials.gov
- No requirement for plain language summaries
- FDA encourages transparent communication
- Good Clinical Practice emphasizes participant respect

Name	Scope	Summary	Resource
FDA Amendments ACT (FDAAA – US federal Law	Clinical trial of FDA regulated drugs, biologics or device products Excludes phase 1 trials and small feasibility studies	Within 12 mo after the primary completion date May be delayed if specific conditions are met, for up to 2 additional yr	Statute (FDAAA 801) 2007 Final Rule (42 CFR Part 11) 2017 FDAAA 801 and the Final Rule | ClinicalTrials.gov
National Institute of Health (NIH) Policy on the Dissemination of NIH-funded Clinical Trial Information	NIH-funded clinical trials of any type of intervention Including Phase1 and feasibility studies	Same as for FDAAA and 42 CFR 11	https://grants.nih.gov/policy-and-compliance/policy-topics/clinical-trials/reporting
Department of Veteran Affairs Office of Research and Development (VA ORD)	Clinical trials funded by the VA ORD	Within 12 mo after the primary completion date	ORD Sponsored Clinical Trials: Registration and Submission of Summary Results

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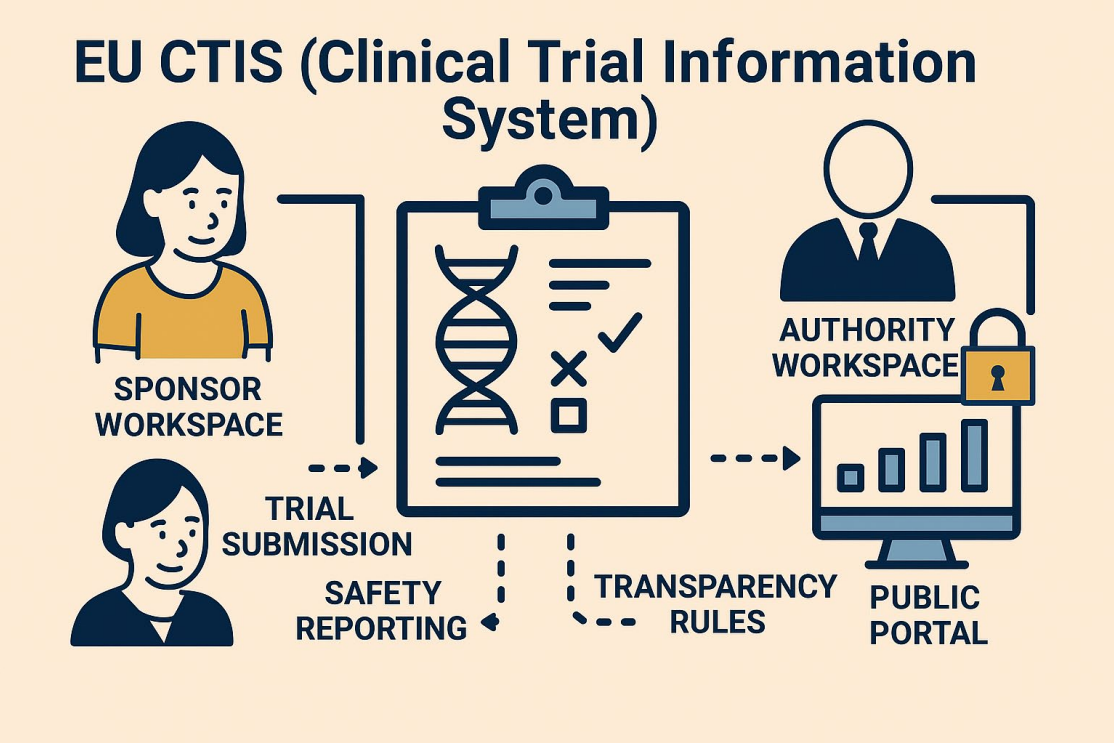
EU Clinical Trials Regulation - EU CTIS[1]

- Lay summaries required for all trials
- Lay summaries for the protocol synopsis and the trial's final and, if applicable, interim results.
- Protocol synopsis and final results within 12 months after study end
- Summaries must be available in local languages of participating member states
- Focus: accessible, clear, patient-centered information



1. Regulation (EU) No 536/2014) https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32014R0536

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Example of Lay Summary from EU CTIS

Clinical Trial Results Summary

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The trial information given in this summary is from one trial only and must not be used to make medical decisions. This drug is not yet approved and the outcomes of this trial may not apply to all patients. Do not change your current medical treatment without consulting your doctor.

Overview

Why was this trial done?

To find out the highest dose of NMS-03592088 that is tolerated and to see how well it works in patients with AML and chronic myelomonocytic leukemia (CMML) that has come back or stopped responding to treatment and who had failed standard therapy.

Who took part in this trial?

Sixty-one adult men and women with AML and CMML that had come back or stopped responding to treatment and who had failed standard therapy.

What treatment was tested in this trial?

All patients who took part in the trial were given NMS-03592088 by mouth.

What were the main results of this trial?

Two patients had dose-limiting toxicities (severe side effects that permitted to define the dose to be used to evaluate if the treatment works in AML patients) in Phase I part of the study. The treatment was therefore evaluated at a lower and safer dose in the Phase II part where 1 patient had complete improvement in the cancer (although without full recovery of healthy blood cells) and 2 patients had morphological leukemia free bone-marrow.

What were the side effects?

The most common side effects were nausea and vomiting. Some patients experienced myasthenic syndrome (a condition that results in muscle weakness). The symptoms observed were all reversible.

What is acute myeloid leukemia (AML)?

AML is the most common type of acute leukemia (cancer of the white blood cells) in adults. NMS-03592088 is a medicine that strongly inhibits the activity of receptors that have an important role in the development of AML, such as FMS-like tyrosine kinase 3 (FLT3). Alterations in the FLT3 gene, specifically the internal tandem duplication (ITD) alteration, are common in patients with AML and can also be found in patients with CMML (a rare type of blood cancer). These alterations are often associated with poor outcomes. Therefore, NMS-03592088 has the potential to prevent cancer from getting worse in patients with AML and CMML.

What was the purpose of this clinical trial?

This trial was designed to answer these questions:

What is the highest dose of NMS-03592088 that is tolerated and what is the recommended dose to be used?

How is the anti-tumour activity of NMS-03592088 in AML patients with the FLT3-ITD alteration?

How was this trial done?

Who took part in this trial?

This trial included treatment of 31 men and 30 women between the ages of 18 to 86 years diagnosed with AML and CMML that had come back or stopped responding to treatment and who had failed standard therapy.

Where did this trial take place?

This trial took place in 4 countries (Italy, Spain, France, and the United States of America), although only 3 of them included patients: 37 patients in Italy; 21 patients in Spain; 5 patients in France.

When did this trial take place?

This trial started in April 2019 and ended in August 2024.

What treatment was tested in this trial?

All patients who participated in the trial received NMS-03592088 in different doses, ranging from 20 to 360 mg/day, by mouth.

What has been completed?

Before treatment, the trial doctor checked the health of every person to ensure they could be in the trial.

The trial was planned to have 2 phases:

- Phase I – NMS-03592088 was administered in different doses to AML and CMML patients to identify the highest tolerated dose and the recommended dose to be used in Phase II. Some patients received NMS-03592088 once daily for 3 consecutive weeks, followed by 1 week of rest in cycles of 4 weeks (Schedule A), while others received NMS-03592088 once daily for 4 consecutive weeks in cycles of 4 weeks (Schedule B).
- Phase II – NMS-03592088 was administered in a fixed dose to AML patients with the FLT3-ITD alteration to see how well it worked. Patients received NMS-03592088 at 360 mg/day for 5 consecutive days, followed by 150 mg/day.

The trial doctor checked for any health issues experienced by the patients at each trial visit and checked for any improvement or regression in cancer regularly. Furthermore, blood tests were done to see how much medicine was in the blood.

What are the main results of this trial?

Overall, the researchers learned that:

In Phase I part of the study, 2 patients had dose-limiting toxicities following administration of NMS-03592088 at the highest doses. The dose-limiting toxicities were symptoms associated with myasthenic syndrome and were reversible.

Five patients in the Phase I part experienced either a complete improvement in their cancer (although without full recovery of healthy blood cells) or had morphological leukemia free bone-marrow.

Based on these safety observations and efficacy (how well NMS-03592088 works in clinical studies) observed in Phase I, a Phase II dose of 360 mg/day for 5 consecutive days followed by 150 mg/day was applied.

In Phase II of the study, 1 out of 9 patients (11.1%) in 1 of the cohorts had a complete improvement in their cancer (although without full recovery of healthy blood cells) and 2 additional patients had morphological leukemia free bone-marrow, following treatment with NMS-03592088.

Information about side effects for the trial can be found in the next section.

These were the **main** results of the trial. More results are included in a detailed report for researchers.

What were the side effects?

Side effects are unwanted medical events thought to be related to the treatment in the trial (NMS-03592088). In this trial, 32 patients (52.5%) had side effects; 7 patients had serious (see definition below) side effects, and 4 patients withdrew the study treatment due to a side effect(s); all these side effects were related to NMS-03592088.

Overall, 2 patients had dose-limiting toxicities, severe side effects that permitted to define a safer dose to be used to evaluate if the treatment works in AML patients. One patient had drooping of upper eyelids which resolved in 4 days after treatment was withdrawn and another patient had shortness of breath, decreased activity, and abnormal posture which resolved in 10 days.

How many patients had serious side effects?

A side effect is serious when one of the below criteria is met:

- The patient needs to be hospitalised.
- The patient's life is in danger.
- It may put the patient at risk and requires medical intervention to prevent the situations listed above.
- It causes permanent damage or death.

In this trial, 7 patients (11.5%) had serious side effects (medical events related to NMS-03592088), each in 1 patient (1.6%): gastric haemorrhage, neurotoxicity, and other symptoms mostly related to myasthenic syndrome such as drooping of upper eyelid, decreased activity, abnormal posture, shortness of breath, and double vision.

In this study, no patient died because of a side effect related to NMS-03592088.

Overall, the most common side effects (reported by at least 4 patients and related to NMS-03592088) were nausea (9 patients, 14.8%), vomiting (7 patients, 11.5%), weakness (6 patients, 9.8%); and high levels of aspartate aminotransferase (blood test), decreased appetite, low levels of neutrophils, and low levels of blood platelets (4 patients, 6.6% each).

What was learned from this trial?

Efficacy was observed with the recommended Phase II dose. Further investigation in AML could aim to increase efficacy and reduce occurrence of myasthenic syndrome.

Where can I find more information about this trial?

For more information about this trial, please visit www.clinicaltrials.eu and clinicaltrials.gov. Results from this trial may be presented in a different way in other documents.

Trial Title	A Phase I/II Study of NMS-03592088, a FLT3, KIT and CSF1R Inhibitor, in Patients with Relapsed or Refractory AML or CMML
Public Trial Title	A clinical trial to explore the safety and the effect of NMS-03592088 in patients with AML and CMML that has come back or stopped responding to treatment
Protocol Number	MKIA-088-001
EU CT Number	2023-508655-39-00
Study Sponsor	Nerviano Medical Sciences, S.r.l. www.nervianoms.com

Please email any questions to clinicaltrials@nervianoms.com.
This study is also registered on www.clinicaltrials.gov **AND** www.clinicaltrialsregister.eu.

Are there plans for further trials?

No further trials are currently planned.

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WHO 2025 Guidance

- Results reported in registries within 12 months
- Eight minimum items required, including PLS
- Summaries should be clear, concise, free of jargon
- Explain purpose, methods, findings, implications

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Pharmaceutical Industry Associations: Principles

- PhRMA & EFPIA support public access clinical study results
- Companies to work with regulators to adopt mechanisms for providing summaries available to research participants
- Initiatives like trialsummaries.com improve access
- Enhances health literacy and engagement

1. Principles for Responsible Clinical Trial Data Sharing | PhRMA, July 25, 2023

PhRMA - ***Ph**armaceutical **R**esearch and **M**anufacturers of **A**merica*
EFPIA – ***E**uropean **F**ederation of **P**harmaceutical **I**ndustries and **A**ssociations*

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Example: GSK

GSK

Ahead Together

As part of our Ethical Scientific Research policy, we commit to developing **Layperson Summaries of Clinical Trial Results** for Phase 2-4 trials of our medicines and vaccines.

We develop summaries within 6 months of study completion for trials in paediatric population and within 12 months for trials in adults.

We translate the summaries into all languages of the informed consent form. This includes rare languages such as Kiswahili, Cyrillic, Dhuluo.

We distribute our summaries to the investigators of our trials to share with trial participants.

We post our Layperson Summaries publicly on:
GSK Study Register: gsk-studyregister.com
Trial Summaries: www.trialsummaries.com

GSK would like to thank all participants and their families for their contribution to the development of our medicines and vaccines

GSK

We follow good writing practices so that our summaries fulfil five key requirements:

Plain Language
Use of simple language to ensure clarity and understanding while keeping the content direct not promoting any product.

Health Literacy Principles
Ensure the text is suitable for all by avoiding technical jargon, unfamiliar words, and complex medical terms.

Numbers and Data
Tailor content to meet the needs of all by presenting whole numbers rather than decimals, using percentages for better understanding when presenting numerical data.

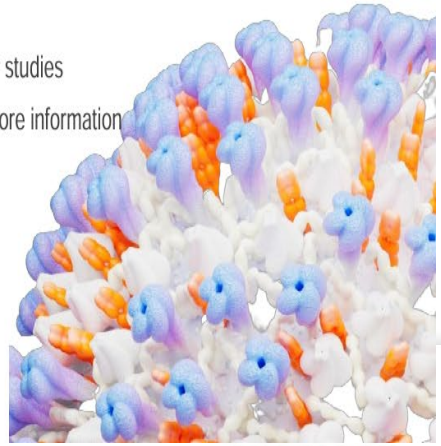
Visual Appeal
Use creative solutions for illustrations of statistical data, results, study designs while striking a balance between visual format and text.

Readability Score
Verify readability score of each summary using well-accepted reading scores such as Flesch-Kincaid Readability score.

GSK

The content of our Layperson Summaries of Clinical Trial Results are aligned to the requirements of the European Clinical Trial Regulation 536/2014 and include:

- ✓ Study names
- ✓ Who sponsored the trial
- ✓ General information about the clinical trial
- ✓ Which participants were included in this trial
- ✓ Which medicines were studied
- ✓ The main results of the trial
- ✓ What the side effects were
- ✓ How the trial has helped participants and researchers
- ✓ Plans for further studies
- ✓ Where to find more information about the trial

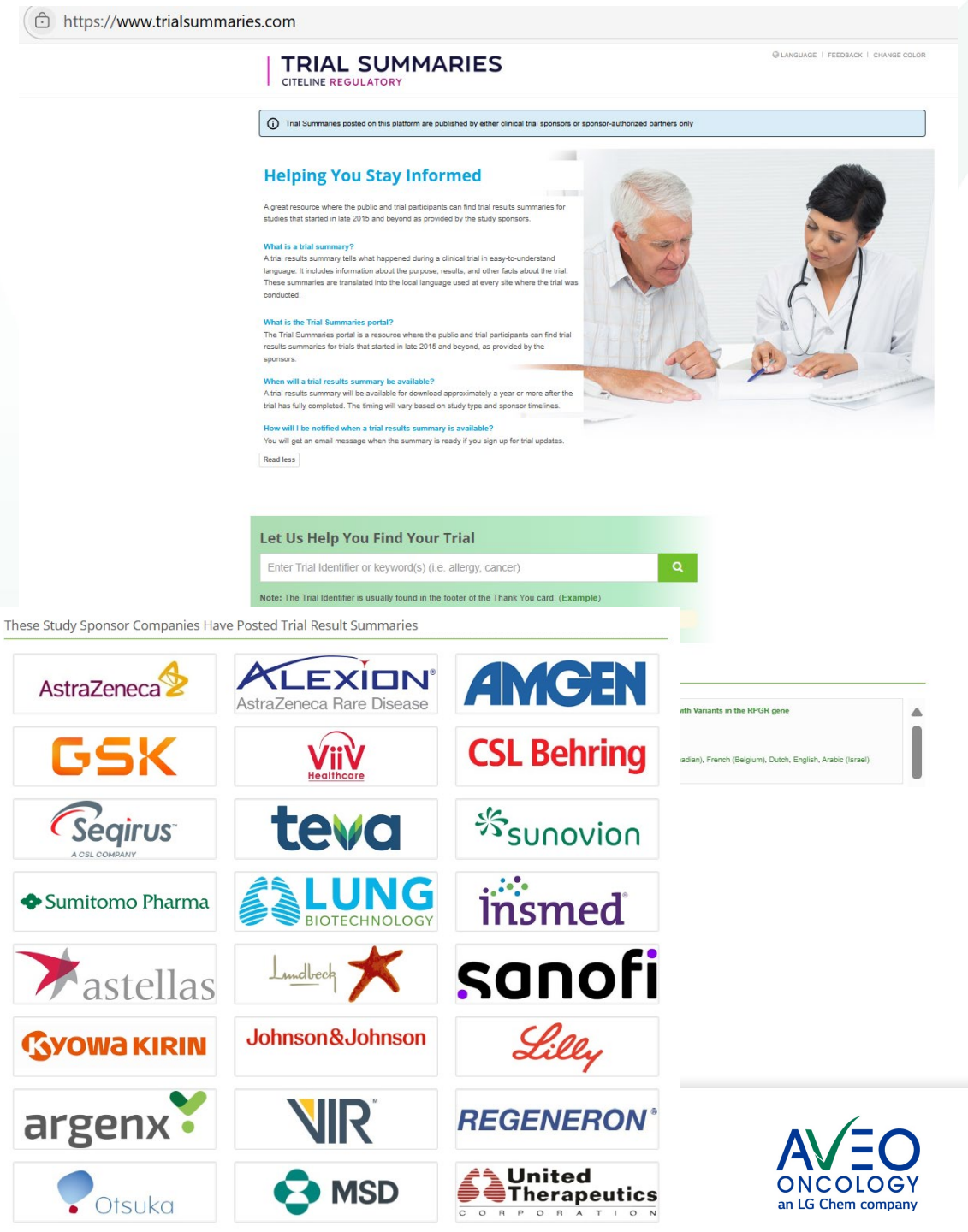


10 November 2023

Trial Summaries

www.trialsummaries.com

- Sponsor-agnostic, publicly accessible site
- Designed to host plain language summaries from multiple pharmaceutical companies
- Aims to improve health literacy and patient engagement by making clinical trial results easier to understand
- Summaries are available in multiple languages while maintaining patient confidentiality



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Summary

- Result-sharing should be standard as a part of study conduct
- Early, planning, patient involvement, and clear, culturally sensitive communication strategies are essential
- Use simple, non-technical language -Offer multiple formats (print, digital, in-person)
- Respect patient autonomy and privacy (opt-in / opt-out options)
- Many countries outside the US require plain-language summary of study results
- Accessible, timely, transparent communication builds trust

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