Webinar Guide:
Deconstructing Clinical Trials

(4:29) A clinical trial involves presenting a therapeutic intervention—which is new, novel, or innovative—to patients with the hope that it will improve upon the current standard of care. Trials aim to test effectiveness, safety, and patient outcomes based on solid preclinical research. Clinical trials can involve new drugs, surgical techniques, radiation therapies, or interventions like screening methods and follow-up protocols. They span the full spectrum of care, from prevention to survivorship. Ultimately, clinical trials aim to advance cancer research and improve quality of life and survival outcomes for patients.

Definitions of Terms

- **Translational Research (07:40):** Research bridging basic science and clinical application (the use of a treatment or technique in patient care) to identify therapeutic targets (specific molecules or cells in the body that treatments are designed to act on).
- **Phase I Trial (08:10):** Early-stage trial focusing on safety, dosage, and pharmacokinetics/dynamics (how drugs move through and affect the body).
- **Maximum Tolerated Dose (MTD) (21:20):** The highest dose of a drug that can be administered safely.
- **Phase II Trial (25:19):** A trial assessing treatment efficacy (how well a treatment works under ideal conditions) in specific conditions.
- **Phase III Trial (25:55):** Large-scale trials comparing a new therapy to the current standard.
- **Statistically Significant (26:32):** A result unlikely to have occurred by chance.
- **Primary Endpoint (29:03):** The main outcome a clinical trial is designed to measure
- **Invasive Disease-Free Survival (IDFS) (29:25):** Time from treatment to recurrence or progression of invasive disease (the spread or worsening of cancer beyond its original site).
- **Secondary Endpoint (30:10):** Additional outcomes measured in a trial to gather more data on a treatment's effects.
- **Kaplan-Meier Curve (33:28):** A graph that tracks how well the clinical trial treatment performed compared to the standard of care. The bottom axis shows time, while the vertical axis represents the primary endpoint (for example, the risk of recurrence). The lines plotted on the graph show the difference between the investigational arm (top line) and the standard of care arm (bottom line).
- **Forest Plot (35:00):** A chart that shows how different groups of patients responded to a treatment. The middle line represents no difference between treatments. If a group's result falls to one side, it suggests they benefited more from the new treatment; if it falls to the other, they did better with the standard treatment.
- **Overall Survival (OS) (30:31) (36:46):** Time from randomization (assigning participants to treatment groups by chance to avoid bias) to death from any cause.
- **Distant Disease-Free Survival (DDFS) (36:30):** The length of time after primary treatment that a patient remains free from cancer recurrence in distant sites, such as bones, liver, or lungs.

- **Progression-Free Survival (PFS) (41:21):** Time from randomization (assigning participants to treatment groups by chance to avoid bias) to cancer progression or death.
- **Real-World Evidence (RWE) (46:08):** Studies analyzing treatment performance in everyday clinical settings.

Types of Clinical Trials:

Translational Research (Bench-to-Bedside): Foundational research conducted in preclinical (research conducted in labs or on animals to test treatments before they are tried in humans) stages to identify potential therapeutic targets (specific molecules or cells in the body that treatments are designed to act on).

- **Example: CAR T-Cell Therapy for Sarcoma**
  (10:33) One example involves a patient, Milan, diagnosed with alveolar soft part sarcoma (ASPS), a rare and aggressive cancer. Translational research identified a target, GPNMB, highly expressed in ASPS. We collaborated with labs to develop a CAR T-cell therapy—a modified T-cell treatment that aggressively targets cancer cells. Preclinical studies in mice showed promising results, leading to Health Canada's approval for a phase I trial in ASPS and triple-negative breast cancer.

Phase I Trials: Early-stage trials testing safety, dosage, and pharmacokinetics/pharmacodynamics (how drugs move through and affect the body) in a small group of healthy or robust patients.

- **Example: Blue Star Study**
  (19:23) The Blue Star clinical trial targets cancers expressing B7-H4 using a bispecific antibody drug conjugate. Phase I trials aim to determine safety and maximum tolerated dose (MTD). Monitoring includes physical exams, frequent blood work, imaging, and genomic studies.

Phase II Trials: Focus on assessing efficacy (how well a treatment works under ideal conditions) in specific cancers.

Phase III Trials: Compare new treatments to the current standard of care with larger patient populations.

- **Example: NATALEE Study**
  (26:32) This phase III trial evaluated the addition of ribociclib to standard endocrine therapy in patients with hormone receptor-positive, HER2-negative early breast cancer. The primary endpoint was invasive disease-free survival (IDFS). Results showed a statistically significant reduction in recurrence for the investigational arm.

Real-World Evidence (RWE): Studies that analyze how approved treatments perform in broader, real-world settings, including patient populations not eligible for traditional clinical trials.

- **Example:**
  (44:48) Real-world studies assess how treatments perform outside of the controlled environment of clinical trials. These studies can be retrospective (analyzing past data) or prospective (collecting new data over time). They help fill gaps in clinical trials by including diverse populations, such as older patients or men with breast cancer, and evaluating long-term treatment sequencing and outcomes.