**Key Takeaways:**

- A novel immunotherapy combination, botensilimab and balstilimab (BOT + BAL), was tested as a treatment for people with metastatic colorectal cancer that failed previous therapies.

- This combination has shown clinical activity and notable overall survival in people without active liver metastases: **23%** had deep, durable responses and **74%** were alive at 1 year.*

- Side effects were manageable and reversible.*

- People with "cold" tumors who normally would not respond to any immunotherapy benefited from BOT + BAL treatment.

- The BOT + BAL combination is currently being tested worldwide in more people with difficult-to-treat metastatic colorectal cancer.

**Novel immunotherapy combination: BOT + BAL**

BOT + BAL is a novel immunotherapy combination being evaluated and has shown clinical activity in "cold" metastatic colorectal cancer. These medicines were specifically designed to harness the power of the person's own immune system to recognize and destroy cancer cells through multiple mechanisms of action:

- **Boosts Immune Response**
  - Primes and expands new T cells that recognize and kill cancer

- **Activates Immune System**
  - Stimulates existing immune cells to more effectively recognize and attack cancer

- **Reduces Immune Suppression**
  - Removes regulatory T cells that suppress the immune response

- **Prevents Recurrence**
  - Establishes "memory" immune cells to combat future cancers

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*Botensilimab and balstilimab are investigational immunotherapies used alone or in combination. These products have not been reviewed and approved by any regulatory agency. Based on data as of May 26, 2023. Presented at the European Society for Medical Oncology World Congress on Gastrointestinal Cancer, 28 June–1 July 2023; presentation number LBA-4.
As of May 26, 2023, 101 people with "cold" metastatic colorectal cancer received BOT (once every 6 wks) + BAL (once every 2 wks).

Notably, 74% of patients without active liver metastases were alive at 1 year. Median overall survival time: ~1.7 years.

Deep and durable responses seen:

- In those without active liver metastases:
  - 69% had ongoing responses, including many lasting more than 1 year.
  - 80% had controlled disease – tumor was no longer detectable, shrunk in size, or was stable.

What do these results mean?

- In this study, the BOT + BAL immunotherapy combination treatment has shown clinical activity and notable overall survival, with manageable side effects in people with heavily pretreated, metastatic “cold” colorectal tumors.
- People with “cold” tumors who normally would not respond to any immunotherapy benefited from BOT + BAL treatment.

What happens next?

- A large, worldwide phase 2 trial called Activate Against Colorectal Cancer (NCT05608044) is currently enrolling to test the BOT + BAL combination in more people with "cold" metastatic colorectal cancer.

People lived longer than reported for standard-of-care:

- Notably, 74% of patients without active liver metastases were alive at 1 year.
- Median overall survival time: ~1.7 years.

Manageable side effects:

- Main drug-related side effects included:
  - 40% Diarrhea / Colitis
  - 32% Fatigue
  - 27% Decreased appetite

- Side effects were manageable and reversible.
- No drug-related deaths and no unexpected side effects.