

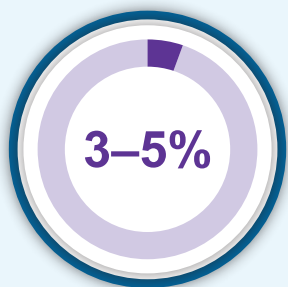
The role of personalised care in cancer of unknown primary



Cancer can form in any tissue of the body. It can also spread to other parts of the body. When cancer spreads it is known as metastasis or metastatic cancer.¹

Sometimes **the metastatic cancer is found but the place where it began (the primary site) is not**. This is called **cancer of unknown primary**, also known as CUP.^{1,2}

There is an urgent need for a better understanding of what causes CUP, to help improve how it is managed.^{2,3}



3 to 5% of cancers are CUP^{2,4}



Not knowing the **original location** of the cancer makes a diagnosis extremely difficult^{3,4}



Treatment is often **limited to chemotherapy**, which can be ineffective^{2,3}

A personalised approach to treating CUP



Most cancer treatments are developed to treat a cancer that has formed in a specific organ or tissue.⁵ Without knowing where the cancer began, it is important to understand the cancer's **genetic information**.³ Two different methods are currently being studied to better understand the genetic information and treat CUP.^{6–11}

- **Comprehensive genomic profiling** tests have the potential to identify biomarkers that can be targeted by existing treatments.^{9–15}
- **Gene expression profiling** tests have the potential to identify the primary site. This can help guide treatment decisions based on where the cancer started.^{6–8,15}

In the future, these methods could help guide decisions about treatment for people with CUP.^{6,8,9,11,15}

This new approach to managing cancer is called precision care. Precision care is an important step towards **personalised care**.^{3,12,17,18}

What are biomarkers?

Biomarkers are molecules found in cells (e.g. genes) that provide important information about a person's cancer.¹⁶ New biomarkers for different cancer types are constantly being discovered.¹⁷

How might genetic testing help manage CUP?^{1,3,6,9–15,19–22}



Biopsy

A tissue or blood sample may be taken – also known as a **biopsy**



Genetic information

Comprehensive genomic profiling can detect multiple biomarkers with a single test

Gene expression profiling tests might support identification of the primary site



Test results

Test results can provide a more complete picture of CUP, to help inform treatment options (but results are not always conclusive)



Personalised treatments

This information might help your doctor identify a **treatment option** either by:

- selecting treatments that can **target biomarkers**, if they are identified (regardless of the primary site)
- selecting treatments based on the **likely primary site** (separate from biomarker testing)

Biomarker testing could become an important part of managing CUP^{9,11,14}



Treatment options for CUP

When CUP is diagnosed, cancer has already spread from one part of the body to another. This means the cancer may be too advanced to be cured. In this case, the aim of treatment is to shrink the cancer to improve symptoms and help people live longer.²² To achieve this, chemotherapy, radiation therapy, hormonal treatments and/or surgery may be used.²²

In the future, genomic testing may help doctors identify biomarkers in some cases of CUP. Based on this information, **targeted treatments** may be selected.^{9–11,14,21,22}



Targeted treatments:

- are directed at **specific biomarkers** that contribute to the growth and spread of cancer²¹
- can be **more effective** and cause **fewer side effects** than traditional treatments (chemotherapy and radiation therapy) because they target specific cancer cells, without harming healthy cells^{12,23}

Examples: angiogenesis inhibitors and cancer growth inhibitors²⁴

What does this mean for me?

Some results from ongoing clinical trials show that targeted treatments may be useful in some people with CUP.²¹

However, currently these new personalised approaches to care for CUP are still being studied.^{6,7,9–11}

More evidence is needed to assess whether these approaches can have sufficient benefit in routine care of CUP.^{6–9,11,15}



Approximately **2** in **4** people with CUP may be able to be treated with existing targeted treatments.²⁵

The future goal is to better understand the genetic information of a person's CUP, so that doctors can choose the best treatment

A diagnosis of CUP can leave you and your loved ones feeling frightened, uncertain and overwhelmed. Keep in the mind the following:

- There are **sources of information and support** for people with CUP.
- **Ask your doctor about testing.** This will help you and your care team understand as much as possible about your cancer and your treatment options.
- **Getting your cancer tested for biomarkers and giving permission to share the information** is also important. If researchers can understand more about the biology of CUP, they may be able to develop more effective care plans or treatments in the future.

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References

1. National Cancer Institute. Carcinoma of unknown primary treatment (PDQ) – patient version. [Internet; cited February 2022].
Available from: <https://www.cancer.gov/types/unknown-primary/patient/unknown-primary-treatment-pdq>
2. Karim Fizazi et al. Cancers of unknown primary site: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*, 2015, Volume 26, Pages V133–V138.
Available from: [https://www.annalsofoncology.org/article/S0923-7534\(19\)47185-8/fulltext](https://www.annalsofoncology.org/article/S0923-7534(19)47185-8/fulltext)
3. European Society for Medical Oncology. Personalised Medicine in Carcinoma of Unknown Primary. [Internet; cited February 2022].
Available from: <https://www.esmo.org/oncology-news/archive/personalised-medicine-in-carcinoma-of-unknown-primary>
4. Giulia Maria Stella, et al. Cancers of unknown primary origin: current perspectives and future therapeutic strategies, *Journal of Translational Medicine*, 2012, Volume 10.
Available from: <https://translational-medicine.biomedcentral.com/articles/10.1186/1479-5876-10-12>
5. Li Yan, Wei Zhang. Precision medicine becomes reality – tumor type-agnostic therapy. *Cancer Communications*, 2018, Volume 38.
Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5953403>
6. Hidetoshi Hayashi et al. Randomized Phase II Trial Comparing Site-Specific Treatment Based on Gene Expression Profiling With Carboplatin and Paclitaxel for Patients With Cancer of Unknown Primary Site. *Journal of Clinical Oncology*, 2019, Volume 37, Issue 7.
Available from: https://ascopubs.org/doi/10.1200/JCO.18.00771?url_ver=Z39.88-2003
7. K Fizazi et al. A phase III trial of empiric chemotherapy with cisplatin and gemcitabine or systemic treatment tailored by molecular gene expression analysis in patients with carcinomas of an unknown primary (CUP) site (GEFCAP1 04). *Annals of Oncology*, 2019, Volume 30, Supplement 5.
Available from: [https://www.annalsofoncology.org/article/S0923-7534\(19\)60360-1/fulltext](https://www.annalsofoncology.org/article/S0923-7534(19)60360-1/fulltext)
8. Elie Rassy et al. The role of site-specific therapy for cancers of unknown of primary: A meta-analysis. *The European Journal of Cancer*, 2020, Volume 127, Pages 118–122.
Available from: [https://linkinghub.elsevier.com/retrieve/pii/S0959-8049\(19\)30874-3](https://linkinghub.elsevier.com/retrieve/pii/S0959-8049(19)30874-3)
9. Jeffrey S Ross. Comprehensive Genomic Profiling of Carcinoma of Unknown Primary Origin: Retrospective Molecular Classification Considering the CUPISCO Study Design. *Oncologist*, 2021, Volume 26, Issue 3, Pages e394–e402.
Available from: <https://academic.oup.com/oncolo/article/26/3/e394/6445517>
10. J J Adashek et al. Personalized molecularly matched therapies for carcinomas of unknown primary is associated with improved outcomes. *Annals of Oncology*, 2020, Volume 31, Supplement 4, Pages S275–S276.
Available from: [https://www.annalsofoncology.org/article/S0923-7534\(20\)40203-0/fulltext](https://www.annalsofoncology.org/article/S0923-7534(20)40203-0/fulltext)
11. Jeffrey S Ross et al. Comprehensive Genomic Profiling of Carcinoma of Unknown Primary Site: New Routes to Targeted Therapies. *JAMA Oncology*, 2015, Volume 1, Issue 1, Pages 40–49.
Available from: <https://jamanetwork.com/journals/jamaoncology/fullarticle/2108853>
12. American Cancer Society. Precision or Personalized Medicine. [Internet; cited February 2022].
Available from: <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/precision-medicine.html>
13. National Cancer Institute. Biomarker Testing for Cancer Treatment. [Internet; cited February 2022].
Available from: <https://www.cancer.gov/about-cancer/treatment/types/biomarker-testing-cancer-treatment>
14. John D Hainsworth, F Anthony Greco. Cancer of Unknown Primary Site: New Treatment Paradigms in the Era of Precision Medicine. *American Society of Clinical Oncology Educational Book*, 2018, Volume 38, Pages 20–25.
Available from: https://ascopubs.org/doi/full/10.1200/EDBK_100014
15. George Pentheroudakis, Alwin Krämer. Genomic profiling clinical trials in cancer of unknown primary. *European Medical Journal Oncology*, 2018, Volume 6, Pages 58–66.
Available from: <https://www.emjreviews.com/oncology/symposium/genomic-profiling-clinical-trials-in-cancer-of-unknown-primary/>

16. My Cancer. What Are Biomarkers? [Internet; cited February 2022].
Available from: <https://www.mycancer.com/resources/what-are-biomarkers>
17. European Society for Medical Oncology. Personalised Cancer Medicine: An ESMO Guide for Patients. [Internet; cited February 2022].
Available from: <https://www.esmo.org/content/download/20122/337223/1/ESMO-Patient-Guide-Personalised-Cancer-Medicine.pdf>
18. Fortunato Ciardiello et al. Delivering precision medicine in oncology today and in future—the promise and challenges of personalised cancer medicine: a position paper by the European Society for Medical Oncology (ESMO). *Annals of Oncology*, 2014, Volume 25, Pages 1673–1678.
Available from: [https://www.annalsofoncology.org/article/S0923-7534\(19\)35106-3/fulltext](https://www.annalsofoncology.org/article/S0923-7534(19)35106-3/fulltext)
19. Jeffrey Gagan, Eliezer M Van Allen. Next-generation sequencing to guide cancer therapy. *Genome Medicine*, 2015, Volume 7, Pages 1–10.
Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4517547>
20. American Cancer Society. Tests for Cancer of Unknown Primary. [Internet; cited February 2022].
Available from: <https://www.cancer.org/cancer/cancer-unknown-primary/detection-diagnosis-staging/how-diagnosed.html>
21. Cancer.net. Unknown Primary: Latest Research. [Internet; cited February 2022].
Available from: <https://www.cancer.net/cancer-types/unknown-primary/latest-research>
22. Macmillan Cancer Support. Cancer of Unknown Primary. [Internet; cited February 2022].
Available from: <https://www.macmillan.org.uk/cancer-information-and-support/cancer-of-unknown-primary/cancer-of-unknown-primary-treatment>
23. Cancer.net. Understanding Targeted Therapy. [Internet; cited February 2022].
Available from: <https://www.cancer.net/navigating-cancer-care/how-cancer-treated/personalized-and-targeted-therapies/understanding-targeted-therapy>
24. Macmillan Cancer Support. Targeted Therapies. [Internet; cited February 2022].
Available from: <https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/targeted-therapies>
25. Roberta Lombardo et al. The Quest for Improving Treatment of Cancer of Unknown Primary (CUP) Through Molecularly-Driven Treatments: A Systematic Review. *Frontiers in Oncology*, 2020, Volume 10, Issue 533.
Available from: <https://www.frontiersin.org/articles/10.3389/fonc.2020.00533/full>