WHAT happens during a genomic test?

A genomic test involves a doctor taking a **tissue sample**, sending this to the lab for **analysis** and then **delivering the results** to you.

The journey of a tissue biopsy

1. Doctor takes a biopsy specimen
2. Specimen is placed in formalin to preserve the tissue
3. Pathologist looks at specimen without a microscope for a first examination
4. Pathologist then embeds the tissue into a wax block and examines it under a microscope
5. Based on the information the tissue reveals, the pathologist either requests additional testing or makes a diagnosis & passes it back to your doctor

So, what happens next?

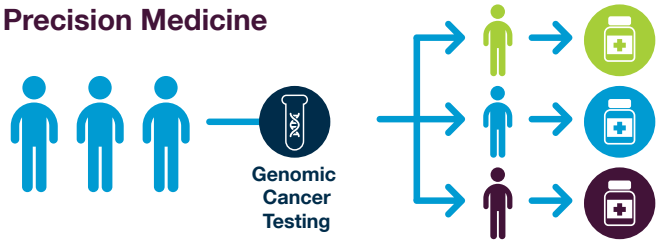
Once your doctor has the results from the labs, he or she will share these with you at your next appointment. If a genomic alteration has been found, this could be a KRAS, HER2, BRAF, EGFR, ALK, ROS1, *NTRK* gene fusion, and many more. Your doctor will go through what the results mean and the next steps.

WHAT is the potential impact on my treatment course?

Each person's cancer diagnosis is different. Yet with traditional cancer medicine, patients have been treated the same. Today, thanks to advances in genomic testing, **doctors can help identify patients that are eligible for precision medicine**.

If diagnosed as eligible through genomic testing, you could be treated **based on your own individual cancer**, with a plan that is based on the genomic alteration. This could mean **fewer treatment courses** to ascertain what works best and **could mean you can start the right therapy earlier**.

Precision Medicine



What if I *don't* have a genomic alteration?

Sometimes, your doctor may not recommend a genomic test for your cancer. Or the results from a test may say that you do not have an actionable genomic alteration, or even an alteration that there is currently no treatment for. In all cases, **you can still discuss the right therapy for you with your doctor, based on the type of cancer you have**.

References

1. Okimoto RA, Bivona TG. Tracking down response and resistance to TRK inhibitors. *Cancer Discov.* 2016;6(1):14-16 **2.** Vaishnavi A, Le AT, Doebele RC. TRKing down an old oncogene in a new era of targeted therapy. *Cancer Discov.* 2015;5(1):25-34 **3.** Mateo J, Chakravarty D, Dienstmann R, *et al.* A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT). *Ann of Onc* 2018;29:1895-1902 **4.** Amatu A, Sartore-Bianchi A, Siena S. *ESMO Open.* 2016;1(2):e000023. **5.** Kumar-Sinha C, Kalyana-Sundaram S, Chinnaiyan AM. Landscape of gene fusions in epithelial cancers: seq and ye shall find. *Genome Med.* 2015;7:129. doi:10.1186/s13073-015-0252-1. **6.** Shi et al. J FGFR1 and NTRK3 actionable alterations in "Wild-Type" gastrointestinal stromal tumors. *Transl Med* (2016) 14:339 DOI 10.1186/s12967-016-1075-6 **7.** Stransky *et al.* The landscape of kinase fusions in cancer. *Nat Commun.* 2014;5:4846. doi:10.1038/ncomms5846. **8.** Gatalica *et al.* Molecular characterization of cancers with NTRK gene fusions. *Mod Pathol.* 2019;32(1):147-153 **9.** Bishop JA, *et al.* Utility of mammaglobin immunohistochemistry as a proxy marker for the ETV6-NTRK3 translocation in the diagnosis of salivary mammary analogue secretory. *Hum Pathol.* 2013;44:1982-1988. **10.** Krings *et al.* Genomic profiling of breast secretory carcinomas reveals distinct genetics from other breast cancers and similarity to mammary analog secretory carcinomas. *Mod Pathol* (2017) 30, 1086–1099 **11.** Yoshihara, K *et al.* The landscape and therapeutic relevance of cancer-associated transcript fusions. *Oncogene* vol. 34,37 (2015): 4845-54. doi:10.1038/onc.2014.406 **12.** Vaishnavi *et al.* Oncogenic and drug sensitive NTRK1 rearrangements in lung cancer. *Nat Med.* 2013;19(11):1469-1472. **13.** Bourgeois JM, *et al.* Molecular detection of the ETV6-NTRK3 gene fusion differentiates congenital fibrosarcoma from other childhood spindle cell tumors. *Am J Surg Pathol.* 2000;24:937-946. **14.** Rubin BP, *et al.* Congenital mesoblastic nephroma t (12; 15) is associated withETV6-NTRK3 gene fusion: cytogenetic and molecular relationship to congenital (infantile) fibrosarcoma. *Am J Pathol.* 1998;153:1451-1458. **15.** Wu G, *et al.* The genomic landscape of diffuse intrinsic pontine glioma and pediatric non-brainstem high-grade glioma. *Nat Genet.* 2014;46:444-450 **16.** Hechtman JF, Benayed R, Hyman DM, *et al.* Pan-trk immunohistochemistry is an efficient and reliable screen for the detection of *NTRK* fusions. *Am J Surg Pathol.* 2017;41(11):1547-1551. **17.** Massard C, Michiels S, Ferte C, *et al.* High-throughput genomics and clinical outcome in hard-to-treat advanced cancers: results of the MOSCATO 01 trial. *Cancer Discovery* 2017;7(6):586-595

MA-LAR-ALL-0138-2
Date of prep: November 2019

BAYER

Understanding genomic testing

& what it could mean for those with cancer

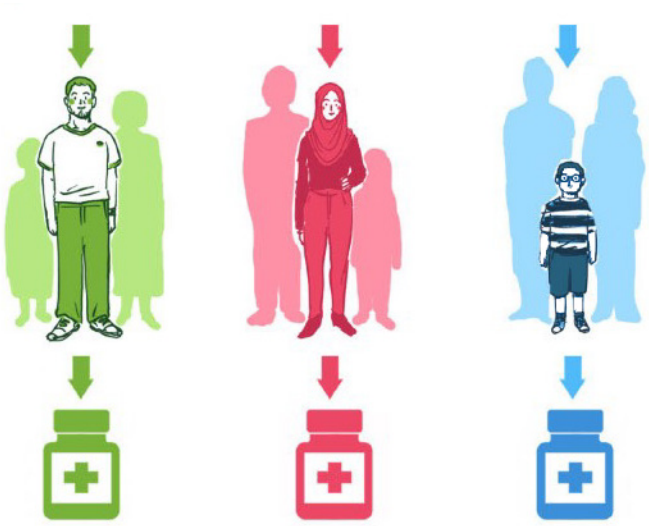
WHY should I ask my doctor about genomic testing?

Cancer used to be defined mainly by where it's located in the body. Now science has shown that some cancers are driven by DNA changes called 'genomic alterations'. **Cancers caused by a genomic alteration** are not limited to certain types of cells or tissues, so can occur in any part of the body. This means that **certain patients with a range of cancers, including rare ones**, such as infantile fibrosarcoma, **could have a genomic alteration** that caused their tumor to grow.[1,2]

The only way to tell if you have a genomic alteration is if your doctor prescribes a genomic test. This can identify a DNA change specific to your tumor, regardless of its location in the body.

A test:

- can **paint a more precise picture** of your individual cancer
- may **provide critical information** that can **guide the course of treatment** prescribed by your doctor

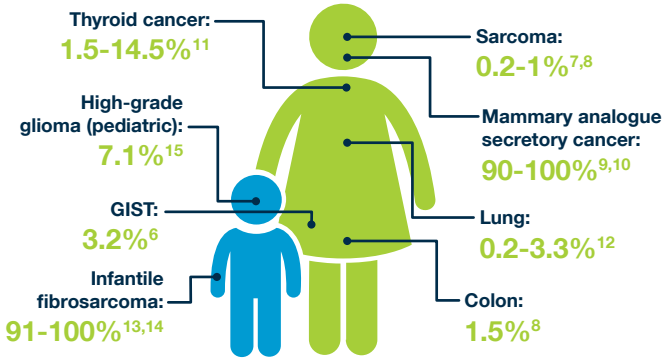


If you're diagnosed with a genomic alteration, **your doctor will better understand the specific drivers of your cancer**, which can then be used to recommend treatments that have been approved or are in clinical trials based on the specific alteration identified. This is called **precision medicine** – a cancer therapy individualized to you.[3]

An example of a cancer caused by a genomic alteration: TRK fusion cancer

TRK fusion cancer is a type of cancer driven by a genomic alteration that can occur in **both adults and children**.[2] It starts with **a rearrangement of DNA in a cell**. A neurotrophic tyrosine receptor kinase *(NTRK)* gene, the one that instructs the coding of TRK proteins, fuses with another gene, and starts producing an altered TRK fusion protein, **driving the growth and spread of a tumor**.[2,4,5]

It is **rare** overall, affecting only **0.5–1% of patients** with solid tumors, but percentages vary by tumor type.[2]



Might I have TRK fusion cancer?

Not all cancers are the same and there are many different reasons why your cancer may have occurred. **The only way to see if your cancer is genomically-driven is if your doctor prescribes a genomic test.**[16]

Studies suggest that **30-49%** of patients with cancer who undergo a genomic test have an actionable alteration,[17] meaning that they can then be linked to an appropriate treatment based on that alteration. If your cancer is caused by any kind of genomic alteration, then it's important for you and your doctor to know this so that **you can get the best treatment options available**.

WHERE do I start?

Genomic testing is not always a routine part of cancer care. If you feel you would like a test, or if you have been recommended one already, here are a few easy steps to help you get started:

Visit testyourcancer.com – this is an educational site for cancer patients, with some key information on testing and its potential benefits

Ask for support – ask a family member, friend or caregiver to accompany you to your appointment

Develop a list of questions to share with your doctor during your appointment. Some examples are below and a full list can be found in the doctor discussion guide at testyourcancer.com:

- Have I had genomic cancer testing?
  - If so, when? What information did it provide about my cancer?
  - Did the test include *NTRK* gene fusions?
  - If not, would genomic cancer testing help us learn more about my tumor?
- Which type of genomic cancer test is best for me?
- What can genomic cancer testing find or identify?
- How is genomic cancer testing different to genetic testing?
- How can the results of a genomic cancer test change my treatment course?

Continue the conversation – care shouldn't end when you walk out of the doctor's office. Make sure to follow-up after your appointment