



## A New Era Has Begun in Cancer Treatment

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The year 2020 is ending, marked by an unprecedented global health, economic and social crisis.

Since the “Spanish Flu”, which was the worst influenza outbreak in history, between 1918 and 1919, which spread at high speed throughout the world and in just 18 months infected a third of the world’s population and claimed the lives of 50 million people, five times more deaths than in the First World War, humanity had not suffered what we are now experiencing, with the COVID-19 Pandemic.

The hope of the entire planet is at this time, deposited in the efficacy and safety of the COVID-19 vaccines, which have recently appeared and have begun to be used.

But life goes on and the rest of the diseases also say “present”, with CANCER being the most prevalent disease in the Western world and the second or third non-infectious disease in other countries, in terms of frequency and mortality.

Fortunately, the fight continues, and we are witnessing a real “explosion” of new drugs in the treatment of cancer diseases.

The knowledge in the molecular biology of cancer, in genetics, in the immunological mechanisms, in the determination of biomarkers and in this new concept of “personalized medicine”, has led to a total change in the diagnostic and therapeutic approach of the tumors, curing more patients, significantly increasing survival in others, making the disease chronic and achieving long remissions with a good quality of life, worth living and with less aggressive, less toxic treatments, most of them with oral formulations, leaving to the much dreaded chemotherapy, as a reminder of the “old cancer treatment”.

Probably, these therapies, called “targeted molecular therapies”, monoclonal antibodies, anti-angiogenics, tyrosine kinase in-

hibitors, immunotherapies, vaccines and the combination of them, even with chemotherapies, are already the new therapeutic arsenal of modern oncology.

### Treatment with molecularly targeted therapy

Extraordinary advances in our understanding of the biology of cancer, including the identification of numerous genetic mutations that fuel tumor growth in certain patients, set the stage for the new era of precision medicine. In this era, the standard of care for many patients is changing from a one-size-fits-all approach to one in which greater understanding of the individual patient and the characteristics of his or her cancer dictates the best treatment option for the patient.

Therapeutics directed to the molecules influencing cancer cell multiplication and survival target the cells within a tumor more precisely than cytotoxic chemotherapeutics, which target all rapidly dividing cells, thereby limiting damage to healthy tissues. The greater precision of these molecularly targeted therapeutics tends to make them more effective and less toxic than cytotoxic chemotherapeutics. As a result, they are not only saving the lives of patients with cancer, but also allowing these individuals to have a higher quality of life than many who came before them.

In the 12 months spanning August 1, 2019 to July 31, 2020, the FDA approved 16 new molecularly targeted anticancer therapeutics (Figure 1). During this period, they also approved nine previously approved molecularly targeted anticancer therapeutics for treating additional types of cancer. For example, in April 2020, the FDA approved the molecularly targeted therapeutic encorafenib (Braftovi) for use in combination with another molecularly targeted therapeutic called cetuximab (Erbix) for treating adults who have metastatic colorectal cancer fueled by a BRAF V600E mutation that has progressed despite prior treatments. This approval followed the approval of encorafenib for treating melanoma, which was highlighted in the AACR Cancer Progress Report 2018.

**Received:** December 29, 2020

**Published:** December 30, 2020

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Approved Indication	Generic Name	Trade Name
<b>CAR T-cell Therapy</b>		
Certain type of non-Hodgkin lymphoma	brexucabtagene autoleucel	Tecartus
<b>Cell-signaling Inhibitors</b>		
Certain types of leukemia and lymphoma*	acalabrutinib	Calquence
Certain type of gastrointestinal stromal tumor	avapritinib*	Ayvakit
Certain type of lung cancer	capmatinib*	Tabrecta
Certain type of colorectal cancer†	encorafenib* and cetuximab	Braftovi and Erbitux
Certain type of bladder cancer	enfortumab vedotin-efv	Padcev
NTRK-positive solid tumors and certain lung cancers	entrectinib	Rozlytrek
Certain type of myeloproliferative neoplasm	fedratinib	Inrebic
Certain type of breast cancer	fam-trastuzumab deruxtecan-nxki	Enhertu
Certain type of bile duct cancer	pemigatinib*	Pemazyre
Tenosynovial giant cell tumor	peixidartinib	Turalio
Gastrointestinal stromal tumor	ripretinib	Qinlock
Certain type of breast cancer	sacituzumab govitecan-hziy	Trodelvy
Certain types of lung and thyroid cancer	seliprecitinib	Retemvo
Neurofibromatosis type 1	selumetinib	Koselugo
Certain type of breast cancer	tucatinib	Tukysa
Certain type of non-Hodgkin lymphoma	zanubrutinib	Brukinsa
<b>Cell Lysis Mediators</b>		
Multiple myeloma	isatuximab-irfc	Sarclisa
Certain type of non-Hodgkin lymphoma	tafasitamab-cxix	Monjuvi
<b>DNA-damaging Agents</b>		
Certain type of bladder and kidney cancer†	mitomycin	Jelmyto
<b>DNA-repair Inhibitors</b>		
Certain types of pancreatic† and prostate cancer†	olaparib*	Lynparza
Certain type of prostate cancer†	rucaparib*	Rubraca
<b>Epigenome-modifying Agent</b>		
Certain types of blood cancer	decitabine and cedazuridine	Inqovi
Certain types of sarcoma and lymphoma†	tazemetostat	Tazverik
<b>Gene-transcription Modifier</b>		
Certain type of lung cancer	lurbinectedin	Zepzelca
<b>Immune-checkpoint Inhibitors</b>		
Certain types of liver† and lung cancer†	ipilimumab and nivolumab	Yervoy and Opdivo
Certain type of lung cancer†	durvalumab	Imfinzi
Certain type of esophageal cancer†	nivolumab	Opdivo
Certain types of skin† and colorectal† cancers and solid tumors that are TMB-H†	pembrolizumab*	Keytruda
<b>Immune-system Modifiers</b>		
Kaposi sarcoma†	pomalidomide	Pomalyst
<b>Nuclear Export Inhibitor</b>		
Certain type of lymphoma†	selinexor	Xpovio
<b>Combinations of Therapeutics That Work in Different Ways</b>		
Certain type of liver cancer†	atezolizumab and bevacizumab	Tecentriq and Avastin
Melanoma†	atezolizumab and cobimetinib and vemurafenib	Tecentriq and Cotellic and Zelboraf
Endometrial cancer†	pembrolizumab and lenvatinib	Keytruda and Lenvima

American Association for Cancer Research (AACR) Cancer Progress Report 2020

Figure 1: Newly FDA-approved anticancer therapeutics: August 1, 2019-JULY 31, 2020.

### Targeting an array of cancers that share the same genetic alteration

One of the most significant precision medicine advances in the 12 months spanning this report was the FDA approval of a second molecularly targeted therapeutic to treat cancer based on the presence of a specific genetic biomarker in the tumor irrespective of the site at which the tumor originated. The therapeutic, entrectinib (Rozlytrek), was approved by the FDA in August 2019 for treating children and adults who have solid tumors that test positive for the NTRK gene fusion biomarker and who have no other options for treatment.

Entrectinib targets three related proteins called TRKA, TRKB, and TRKC. The genes NTRK1, NTRK2, and NTRK3 provide the code that cells use to make these proteins. Entrectinib also targets two other proteins, ROS1 and ALK.

Research has shown that genetic alterations known as chromosomal translocations that involve the three NTRK genes and lead to the production of TRK fusion proteins drive the growth of up to 1 percent of all solid tumors [1].

These solid tumors encompass a wide array of cancer types that occur in adults and children, including many rare cancers, such as mammary analogue secretory carcinoma of the salivary gland, infantile fibrosarcoma, and cholangiocarcinoma.

Entrectinib was approved based on combined data from several phase I and phase II basket trials [2].

The data showed that 57 percent of patients treated with the molecularly targeted therapeutic had complete or partial tumor shrinkage. Tumor shrinkage was seen across a range of cancer types, including NSCLC, mammary analogue secretory carcinoma of the salivary gland, breast cancer, colorectal cancer, thyroid cancer, pancreatic cancer, and sarcomas.

Thus, as we want us to quickly vaccinate the entire world population and achieve the long-awaited immunity, we also hope that in the coming years, more and better molecules will help cancer patients achieve a higher cure rate and preventive measures will slow down. this other underhanded pandemic, silent, deadly many times, but present and more current than ever, which is cancer.

### Bibliography

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2. RC D., *et al.* "Entrectinib in Patients With Advanced or Metastatic NTRK Fusion-Positive Solid Tumours: Integrated Analysis of Three Phase 1-2 Trials". *Lancet Oncology* 21.2 (2020): 271-282.

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