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What a Day in Medicine!!

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INTRODUCTION

Science amazes us every day, whether it's a call from your beloved from thousands of miles away , your favorite program on TV aired from faraway places , your coffee machine that makes your delicious cup of coffee, your car, your laptop, internet, wireless connectivity , Alexa/Google/Siri ,Social media, AI applications and what not! We are so much used to these luxuries that we fail to stop for a second to realize how awesome they are.

On 15th of February, an awesome thing happened in medical science also. I happened to come across a news article from the Gustave Roussy cancer centre in France where a 13 year old child defied all the odds and is the first ever pediatric case to win a battle against a deadly brainstem tumor called Diffuse Intrinsic Pontine Glioma (DIPG).He has been receiving treatment from the Gustave cancer center under the BIOMEDE study for DIPG, with observation of Dr. Jacques Grill who, on 14th – 15th of February 2024 confirmed that patient's tumor had completely disappeared on his recent MRI scan ! What a news, Right!!

WHAT IS "DIPG"??

If you are not from the medical community, I can totally understand the anxiety and the lack of clarity associated with BIG words like "tumor" "DIPG" or "BIOMEDE TRIAL" etc. but don't worry, as a doctor, I shall help you to understand these terms better so that you can have a clearer understanding of the topic that we are about to discuss.

DIPG: This term, when expanded, describes itself i.e. Diffuse (one that is not localized) Intrinsic Pontine(i.e. the tumor belongs to the pons) Glioma (tumor of glial cells of brain) .

Glial cells are the supporting cells of the central nervous system and are of three types i.e. microglial cells , astrocytes and oligodendrocytes. Microglial cells protect our CNS against infections, similar to macrophages in our body. Oligodendrocytes are the cells which cover some of our CNS axons with myelin sheath and astrocytes are the cells that support the network of neurons and help in healing after an injury. They (astrocytes) also maintains the optimum chemical environment for the neurons to work at their best and also regulates the Blood Brain Barrier (BBB). Hence astrocytes are extremely important component of our CNS tissue.

DIPG belongs to category of fibrillary astrocytoma family. [**Source:** https://www.ncbi.nlm.nih.gov/books/NBK560640/]

Signs and Symptoms of DIPG:

DIPG progresses rapidly with symptoms like diplopia, facial nerve paralysis/weakness, cerebello-pontine connection related signs like dysarthria, dysmetria and ataxia. Hydrocephalus is also reported in few cases.

Most patients experience a triad of symptoms which include long tract signs, cerebellar signs and cranial nerve neuropathies.

Source of above information

(https://www.ncbi.nlm.nih.gov/books/NBK560640/)

It is important to tell here that even if above symptoms are present, still the diagnosis of DIPG has to be confirmed.

BIOMEDE STUDY

BIOMEDE stands for the Biological Medicines for Diffuse Intrinsic Pontine Glioma Eradication and is a very interesting approach of clinical study done till date.

In this study, patients whose radiological imaging are suspicious of DIPG are enrolled and their diagnosis is first confirmed with stereotactic biopsy. Now, I should tell you the importance of this step.

DIPG is a kind of tumor that is not localized but it is diffuse, hence doctors used to avoid biopsy for the diagnosis and rely on findings of the radiological imaging to avoid any damage to the pons tissue as a result of the biopsy process. But it has been found that sometimes the radiological imaging shows false positive results i.e. another tumor/condition misdiagnosed as DIPG. So it was of immense importance to the researchers that the diagnosis of the DIPG is confirmed by pathological and histological means and only after the confirmation they would let the patient participate in the study .It is essential for the validation of the study but more importantly it is crucial for the health of the patient as delay in the required treatment can result in worst health implications.

After confirmation of the diagnosis and completing the required documentation and other work, the BIOMEDE study was started and followed for a median period of 5.3 years. You can know about the whole study, requirements and recruitment and ethical guidelines by reading the whole paper

of Dr Jacques Grill and team (Gwenael Le Teuff, Pascale Varlet, Darren R. Hargrave, Karsten Nysom, Klas Blomgrenn, Geoffrey Brian McCowage, Francisco Bautista, Dannis Van Vuurden, Marie-Anne Debily, Thomas Kergrohen, Stephanie Puget, Stephanie Bolle, Samuel Abbou, Pierre Leblond, Nathalie Boddaert, Gilles Vassal, and Marie-Cecile Le Deley).

Here is the link of the abstract of the whole paper https://doi.org/10.1200/JCO.2023.41.16_suppl.10003

What is so special about BIOMEDE??

Now, that we know what BIOMEDE is,let me explain it to you the uniqueness of this trial .

First of all, the pediatric patient, who was enrolled under this trial showed miraculous results which have never been obtained with any other ongoing research for the cure of DIPG in any patient before. In the words of Dr Grill "Lucas's tumour had an extremely rare mutation which we believe made its cells far more sensitive to the drug," [**Source:** https://english.ahram.org.eg/NewsContentP/7/517748/Life--Style/First-child-cured-of-rare-brain-tumour-%E2%80%98offers-rea.aspx].

The patient was only 6 years old (DIPG usually affects children of age group between 5 to 10 years) **(source**: https://www.ncbi.nlm.nih.gov/books/NBK560640/) and now at age of 13 years i.e. after 7 years, patient's MRI shows no trace of residual tumor. Dr Jacques Grill's joy knew no boundary when he witnessed these results, consistently watching the tumor shrink over the years and then one day, it's completely gone. The 6 year's old little boy who was expected to live for a few months only has won a deadly battle. And now because of these results, we are hope full for the future of the promising treatment for DIPG.

BIOMEDE trial has a unique approach which has been termed as "targeted therapeutic approach". In this research, the tumors [DIPG with H3K27me3 loss (with or without H3K27M mutation)] are targeted by radiotherapy and one of the three drugs i.e. erlotinib, everolimus, and dasatinib. These drugs are based on the molecular profiling of the tumor of the patient.

Let's take the drug erlotinib. Erlotinib is a tyrosine kinase inhibitor and it inhibits the intracellular phosphorylation of tyrosine kinase which is associated with the Epidermal Growth Factor Receptor (EGFR)

[Source:https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021743s010lbl.pdf] .

"The randomization was designed so that a drug could not be allocated if the corresponding biomarker was absent in the tumor (EGFR overexpression for erlotinib, mTOR activation for everolimus, no specific biomarker for dasatinib)."

[**Source:**

https://doi.org/10.1200/JCO.2023.41.16_suppl.10003]

After the completion of the study, it was found out that the Everolimus had an upper hand in terms of lesser reports of toxicities experienced by the patients and better overall median survival rate.

BIOMEDE 2.0:

Year 2022 provided us with yet another good news! The recruitment for the BIOMEDE trial 2.0 began and is still going on. This time, the two drugs Everolimus and ONC201 will be under study and the results will be based on the profile for PFR i.e. Progression Free Survival.

The Study started in September 2022 and is estimated to achieve its primary completion in September 2028. If you want to know more about this new study in detail and other criteria like eligibility and non-eligibility you can find this study on the given link

https://classic.clinicaltrials.gov/ct2/show/NCT05476939 .

SUMMARY

It might not appeal to some people as a big advancement in science unlike the newest technologies in the entertainment industries but to me, as person of science it is crystal clear that this research can lay down roads to big potentials in medical science. This won't only lead to the better in-depth understanding of the pathology but would also help emerge new treatments with almost 99% response rate and fewer side effects.

A 13 years old's victory has provided a huge motivation to the whole medical community and we are all waiting eagerly for the results of BIOMEDE 2.0.

REFERENCES

I would like to extend my warmest regards and hearty congratulations to the whole hardworking team at Gustave Roussy Cancer Center France who put their day and night and achieved successful results with their BIOMEDE Study. I extend my heartfelt best wishes to Dr Jacques grill and team (Gwenael Le Teuff, Pascale Varlet, Darren R. Hargrave, Karsten Nysom, Klas Blomgrenn, Geoffrey Brian McCowage, Francisco Bautista, Dannis Van Vuurden, Marie-Anne Debily, Thomas Kergrohen, Stephanie Puget, Stephanie Bolle, Samuel Abbou, Pierre Leblond, Nathalie Boddaert, Gilles Vassal, and Marie-Cecile Le Deley) and all others involved .

I first got to know about this news on Ahram Online (https://english.ahram.org.eg/NewsContentP/7/517748/Life--Style/First-child-cured-of-rare-brain-tumour-%E2%80%98offers-rea.aspx) and I am thankful to them for reporting this important piece of information to the world.

Rest all of the links have been mentioned in the article itself at their appropriate places

I shall try to keep a look out on the developments and progression of the BIOMEDE 2.0 STUDY with full enthusiasm and positivity. My best wishes are with the team of BIOMEDE 2.0 [SPONSORS: Gustave Roussy, Cancer Campus, Grand Paris] and others.

I should inform my readers that there is always space to learn and we all never stop learning especially the persons of medical science community, like me .I extend my apologies in advance if my understanding has few errors and I welcome

any kind of input and correction that my readers might think are important .I always encourage healthy criticism and respect your valuable opinion .

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