Answering T.T.P.
Thrombotic Thrombocytopenic Purpura Foundation

Key Message Document

The following document is a set of key messages that you can use in your conversation with your local MPP. You do not need to make sure that everything in this document is explained to your MPP, rather – use these messages as a way to build a story to someone who does not know what aTTP is and why you are in their office (in person or virtually) to speak to them today.

What is TTP?

Thrombotic Thrombocytopenic Purpura (TTP) is a serious and rare blood disorder with life-threatening medical effects that, if left untreated, is fatal.

- There are two types of TTP: 1% are hereditary TTP (hTTP) and 99% are acquired TTP (aTTP).
- aTTP is an autoimmune disorder that results in the deficiency of the ADAMTS13 enzyme. A deficiency of this enzyme can cause small blood clots to form throughout the body and prevent oxygen and blood flow to critical organs and cause damage.
- TTP is an unpredictable episodic condition that is not well understood and while some TTP patients may only face one episode in their lifetime, others can face numerous episodes with no knowing of when it may happen again.
- The medical community has characterized an aTTP crisis as a true medical emergency because damage to critical organs from the small blood clots happens quickly, is unpredictable, life-threatening, and can be irreversible. The first symptom of aTTP that brings a patient to an ER could be as serious as a stroke. Less severe signs of TTP include fatigue, fever and bleeding to neurologic symptoms and bruising.
- The small blood clots that characterize this disease can have sudden and severe consequences, but because standard therapies are not targeted and take time to "kick –in", patients are left in a life-threatening state for days and sometimes weeks. During this time up to 20% of patients die and others are left with life altering complications from stroke, heart attack etc.[1].

[1] Pavenski K et al. Efficacy of Caplacizumab in patients with aTTP in the HERCULES study according to initial immunosuppression regimen. Blood. 2019;134 (Supplement 1): 2365

Who does aTTP affect?

aTTP is a rare disorder that afflicts 2-6 people per million[2], however a TTP episode is ALWAYS a matter of life and death.

- Each aTTP crisis can cause lengthy hospitalizations, disable, or even be fatal to an aTTP patient. Many patients stay an average of 9.7 days in the intensive care unit and an average of 14.4 days in hospital.[3]
- Without effective and timely treatment, 95% of patients succumb to the disease; however, with treatment 80% - 90% of aTTP patients enter into remission[4]. 30% of these patients entering remission will relapse.[5]
- aTTP can strike people of all ages, but usually young women. Many of these women have young families and promising careers. When a TTP episode occurs, immediate medical intervention is required.

What is the current standard of care for aTTP and why isn't the current standard of enough?

- The current standard of care for aTTP is plasma exchange and immune suppression. Plasma exchange is a frightening, risky, and unpredictable treatment. Utilization of this untargeted treatment dates back to the 1980s. The treatment replaces a patient's blood plasma in an attempt to rebalance enzyme levels and remove antibodies. This untargeted treatment is repeated at least daily and then tapered-off as tolerated. Sudden life-threatening flares during tapering, or soon after, is not uncommon and requires the process to start again with daily treatments. Plasma exchange can only be administered to hospital in-patients and may require weeks and sometimes months of hospital stays. For the duration of this time, the patient remains at risk of severe complications and death.
- Being at risk of life threatening/altering complications and having your entire volume of blood exchanged through a machine, via a catheter that protrudes through a hole in your neck, chest or thigh, for 2-4 hours on a daily basis (sometimes twice a day) for weeks or months, takes not just a physical toll, but a long-lasting emotional toll on patients and families.
- If advancement in treatments reduce the risk of death/irreversible consequences from each TTP crisis, patient's mental health during remission will improve. The uncertainty of the severity and timing of the next relapse brings about real mental stress. A high prevalence of PTSD and depression in TTP survivors has been reported and a study found that 80.8% of individuals with TTP have mild depressive symptoms, compared 10.5% found in the general population.[6]

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[2] Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura. Journal of Thrombosis and Haemostasis : JTH. 2020 Oct;18(10):2486-2495. DOI: 10.1111/jth.15006

[3] Scully M, Cataland SR, Peyvandi F, et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. N Engl J Med. 2019;380:335–346 DOI: 10.1056/NEJMoa1806311

[4] Pavenski K et al. Efficacy of Caplacizumab in patients with aTTP in the HERCULES study according to initial immunosuppression regimen. Blood. 2019;134 (Supplement 1): 2365

[5] [2] Kremer Hovinga J et al. Survival and relapse in patients with thrombotic thrombocytopenic purpura. Blood 2010; 115(8):1500-1511https://doi.org/10.1182/blood-2009-09-243790

[6] Chaturvedi S, Oluwole O, Cataland S, McCrae KR. Post-traumatic stress disorder and depression in survivors of thrombotic thrombocytopenic purpura. Thromb Res. 2017 Mar;151:51-56. doi: 10.1016/j.thromres.2017.01.003. Epub 2017 Jan 6. PMID: 28113083

What is caplacizumab and why does the TTP community need it?

- Caplacizumab is indicated for treatment of aTTP that, when added to the standard of care, is proven to prevent blood clots from forming in the body. This allows patients to recover from aTTP episodes quicker, and with a lower risk of damage to organs and other long-term disabilities associated with aTTP.

What is the TTP community's ask? Why am I meeting with the MPP today?

We are seeking access to caplacizumab for aTTP patients identified by their physicians to benefit from it.

Caplacizumab was granted a *priority review* and approved by Health Canada in March 2020. Caplacizumab is the first new treatment for acquired TTP in about 25 years with a different mechanism to the other drugs and treatments that form the current standard of care.

- A priority review status indicated that Health Canada believed it would be in the best interest of Canadians to review a potential life-saving drug in almost half the review time it takes for other drug reviews (180 day target versus 300 days for non-priority drugs).
- In April 2020, Quebec's INESS (Institut national d'excellence en santé et services sociaux) issued a negative recommendation.
- In September 2020, Canadian Agency for Drugs and Technologies in Health (CADTH)'s Common Drug Review issued a negative recommendation for caplacizumab citing issues with the clinical trial design.
- Caplacizumab was recommended for reimbursement by the National Institute for Health and Care Excellence (NICE) in the UK with the same clinical study submission sent to CADTH. CADTH and NICE have a long track record of working together, including supporting efforts for Early Scientific Advice for new and breakthrough therapies.
    - Despite sharing concerns on several issues raised by CADTH including limitations in the manufacturer's trial model, NICE recognized the value of caplacizumab to aTTP patients.
    - NICE recognized that the benefits of the drug outweighed some of the questions it had in its cost-effectiveness estimates. This included reducing the use of scarce resources such as plasma or ICU beds, both of which (province) should consider as COVID-19 has not only limited hospital budgets, but global plasma levels remain low and in demand.
    - With a clinical positive recommendation, NICE allowed for the manufacturer to provide economic incentives (discounts) for public reimbursement. Unfortunately, the negative clinical recommendation from CADTH does not allow for this option to be considered.
- Canada is an outlier when it comes to coverage and reimbursement for caplacizumab: the treatment is currently covered for patients with aTTP in peer countries such as the United States, Austria, Belgium, Denmark, Netherlands, Finland, Italy, and the UK.

***We want** (insert province) to fund access to caplacizumab **for the subset of patients identified by their physician to benefit from treatment** – namely, those who do not respond to the current standard of care or are otherwise compromised by other conditions or complications.*