Penn Medicine

CLINICAL BRIEFING™

Penn Neurology • Penn MS Center

Kesimpta® (Ofatumumab) for Relapsing Multiple Sclerosis

The Multiple Sclerosis and Related Disorders Center at Penn Medicine is among the first in the region to offer access to Kesimpta (ofatumumab), a monoclonal antibody (mAb) for the treatment of adults with relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. Recently approved by the FDA, Kesimpta is a once monthly subcutaneous injection that is self-administered by patients who receive counseling and injection guidance from a healthcare professional.

Chief of the Multiple Sclerosis Division at Penn Medicine, Amit Bar-Or, MD, FRCPC, played a key role in the development leading to approval of Kesimpta as the principal investigator and lead author for the Phase II MIRROR study published in *Neurology,*[1] and as steering committee member and co-author of the Phase III ASCLEPIOS trials of ofatumumab recently published in the *New England Journal of Medicine.*[2]

A chronic autoimmune disorder of the central nervous system, MS has long been thought to be mediated predominantly by activated T cells (CD4 and CD8) with a presumed specificity for myelin antigens. The T cells are thought to release pro-inflammatory cytokines that activate other cells including microglia, the resident immune cells of the CNS, together promoting further inflammation, myelin injury and plaque formation in the CNS.

It is now known that B cells also play key roles in mediating pro-inflammatory responses in MS. In addition to driving humoral immunity, B cells (and particularly memory B cells) participate in antigen presentation to activate T cells, provoking the aforementioned impact on the CNS. B cells express CD20 and, as a consequence, mAbs that target CD20 (including ofatumumab) and deplete circulating B cells, have become an important therapeutic intervention for MS.

About Kesimpta

Kesimpta is a fully human anti-CD20 antibody previously indicated for the treatment of chronic lymphocytic leukemia (CLL). In patients with MS, the agent is self-administered subcutaneously at a lower dose than that used for CLL. Once injected, ofatumumab binds to the CD20 molecule on the B-cell surface (in a region distinct from that of other anti-CD20 antibodies), to induce potent B-cell lysis and depletion, and appears to have a high binding affinity and long binding duration. In two recent comparative Phase III trials, ofatumumab was associated with lower annualized relapse rates than teriflunomide among patients with MS.

Kesimpta at the Penn MS Center

The Penn MS team is comprised of a full spectrum of healthcare professionals with diverse skills and roles who support the unique needs of the MS patient population, including pharmacists who specialize in MS and the many specialty medications that are prescribed for MS treatment. The MS team pharmacists counsel each patient when a new medication is initiated, and collaborate with MS nurse practitioners and physicians to conduct virtual and in-office visits for Kesimpta® injection training and patient self-administration of the first dose.* Once patients are established on therapy, the team works together to monitor required labs and patient outcomes, as well as follow-up counseling. Patients also have access to a social worker, nursing team, family planning specialists, and other essential professionals trained in the treatment of MS.

*The first injection is performed under the guidance of a healthcare provider (HCP), whether in office or virtually over telemedicine, on the basis of what the HCP feels is medically appropriate and necessary.

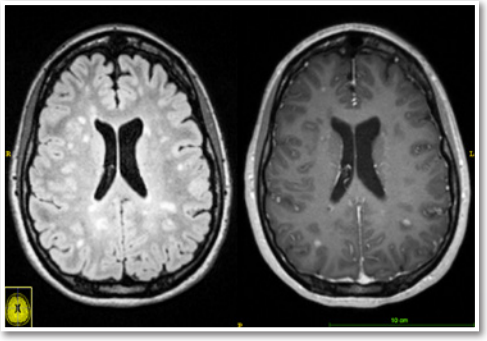

Figure 1: T2 hyperintensities and gadolinium-enhancing lesions in the supra- and infratentorial regions of the brain.

CASE STUDY

Ms. M, is a 28-year-old previously healthy female who awoke one morning to a sensation of intense burning over her left eye. Over the next day, the burning slowly spread to her left temple, cheek and upper left lip. Suspecting shingles, Ms. M's PCP prescribed valacyclovir, and within two weeks, her symptoms slowly subsided. Eighteen months later, however, Ms. M had sudden onset left-sided facial weakness accompanied by dysarthria. Alarmed, and afraid that she might be having a stroke, she went to a local ER.

Finding no evidence of stroke, fever, or infection and normal routine labs, the ER referred Ms. M to a neurologist, and she went home. At her neurology visit two days later, she reported continuing left-sided facial numbness and irritation. A contrast-enhanced MRI of her brain and spine was scheduled. This showed several T2 lesions and gadolinium-enhancing lesions approximately 3mm in size in both the supra- and infratentorial regions. No cervical or thoracic cord lesions were noted. A spinal fluid analysis revealed normal cell counts, glucose and protein, but detected 4 unique oligoclonal bands. The diagnosis of relapsing remitting MS (RRMS) was made.

Ms. M began a course of subcutaneous interferon beta-1b, and her symptoms subsided again. Several months later, she experienced a prolonged period of lassitude and fatigue culminating in a fall on the stairs in her home.

(Continued on back)

CASE STUDY *(Continued)*

Her neurologic examination revealed mildly increased tone in her right leg, decreased vibratory and proprioceptive sensation in her feet, a positive Romberg, and mild gait ataxia. These were new clinical findings. A second MRI was performed, and two new lesions were noted, one in the brain and one in the thoracic spine, which was enhancing.

At this point, Ms. M was advised to change her disease modifying therapy, as she had clinical and radiological evidence of disease activity. She was also found to have a positive JCV antibody test.

After expressing concern about the risk of progressive multifocal leukoencaphalopathy (PML) with natalizumab, it was recommended that she start a B-cell depleting agent, either ocrelizumab (Ocrevus) or ofatumumab (Kesimpta). Both options were discussed with Ms. M, who noted that she might be relocating for a new job opportunity in the next few months and was concerned about starting an infusion therapy and having to switch infusion sites. She felt it would be more convenient and easier to access the medication if she started Kesimpta, a monthly injection that she could be trained to do on her own. In advance of starting the Kesimpta, she had screening laboratory studies, including a negative hepatitis B panel, normal CBC and hepatic function studies.

The Penn MS Center Pharmacy team met with Ms. M and explained the treatment to her, and the nurse practitioner team completed the first dose injection with her in clinic to observe for possible side effects. She tolerated the Kesimpta well and continued it. Her next examination three months later revealed improvement in her vibratory and proprioceptive sensory loss and improvement of her gait ataxia to baseline. A follow-up MRI at that point revealed resolution of the enhancement of her spinal cord lesion and the absence of new lesions.

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References
1. Bar-Or A, Grove RA, Austin DJ, et al. Neurology 2018;90:e1805-e1814.
2. Hayuser SL, Bar-Or A, Cohen JA, et al. N Engl J Med 2020;383:546-57.

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FACULTY TEAM

Recognized by the National MS Society as a National MS Comprehensive Care Center, the Penn Multiple Sclerosis and Related Disorders Center is a nexus for MS clinical research and comprehensive care. The Center is made up of an expert team that includes MS physicians, social workers, advanced practice providers, nurses and researchers, and is also the only facility in the region to offer the services of dedicated MS pharmacists.

The Penn MS Center is located at Perelman Center for Advanced Medicine (PCAM), and recently expanded to the new Penn Medicine Radnor, offering the same level of diagnosis, care and treatment at this convenient location.

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