<table>
<thead>
<tr>
<th>Date Issued</th>
<th>July 27th, 2016</th>
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<tr>
<td>Deadline for application</td>
<td>August 26th, 2015</td>
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<tr>
<td>Award(s) Announced</td>
<td>By September 1st, 2016</td>
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<tr>
<td>Therapeutic Area</td>
<td>Gastroenterology-IBD</td>
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<tr>
<td>CGA Identifier</td>
<td>CGA-IBD-CCFA 2016 symposium Please reference this code in the “Activity Title” field on the Takeda Educational Grant online application form.</td>
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**Purpose of Call for Grant Application (CGA)**

To increase health care professional knowledge and skills related to:

- Risk/benefit of existing anti-integrin therapies for IBD
- Real world treatment patterns of IBD with anti-integrin biologics
- Clinical trial data related to pipeline anti-integrin therapies for IBD

**Summary of Health Care Gap**

Data gathered from sources outside of randomized controlled trials reflecting the actual experiences of patients is referred to as real-world data and is derived from sources such as: clinician and hospital electronic health records, lab information systems, administrative claims systems and registries. There is a growing consensus that real-world data should play a significant role in supporting and strengthening the evidence base for safety and effectiveness of available therapies. (1)

Real world data also plays a significant role in an era of personalized medicine to treat Inflammatory Bowel Disease (IBD). By systematically collecting data about symptoms and response to medications, healthcare settings may provide the ability for both patients and their clinicians to look for patterns that could lead to more effective treatment of IBD, to attain the goal of achievement and maintenance of remission (2,3).

In the last 15 years, the main progress in the field of IBD has been related to development of biologic agents including anti-TNF’s. However, approximately 20% of patients do not respond to anti-TNFs, and over 30% eventually lose response. In addition, these drugs have been shown to increase the risk of infections and malignancies. This along with the increased understanding of the pathogenesis of the inflammatory process in IBD, have led to the development of new anti-integrin biologic therapies (natalizumab, vedolizumab, and entolizumab) deploying innovative mechanisms of action. (3, 17, 18).

Natalizumab was shown to induce and maintain remission in patients with moderate-to-severe CD. Natalizumab however was found to increase the risk of progressive multifocal leukoencephalopathy (PML, approx. 1/300 patients), a central nervous system JC virus infection that can be lethal due to impaired central nervous system immune function. (18, 19).

Clinical trials for vedolizumab illustrated effectiveness and safety for induction and maintenance in moderate to severe UC and CD. A network meta-analysis showed that in patients with moderate-to-severe UC, naïve to biologics, vedolizumab has similar efficacy to infliximab, adalimumab and golimumab, for induction and maintenance. Only vedolizumab had a lower incidence of serious adverse events compared with placebo (20,21).
Additional post approval IBD studies conducted globally have illustrated evidence of vedolizumab therapy on improved clinical remission rates (including steroid free clinical remission), disease activity, mucosal healing, treatment persistence, health related quality of life (HRQoL) and reductions in hospitalizations and surgeries. (4-16)

Etrolizumab is another anti-integrin, currently being investigated in phase 3 trials for UC. Phase II studies with etrolizumab demonstrated 21% remission rates of UC patients at 10 weeks compared to 0% for placebo. That with optimal dosing, remission rate is approximately 20%. Data on mucosal healing and response in anti-TNF failure patients has not been reported. (18,22)

Other anti-integrin therapies still under development are, AJM300, AMG 181 and Ptg-100. AJM300 was shown to be well tolerated and more effective than placebo in inducing clinical response, clinical remission, and mucosal healing in patients with moderately active UC. (24) A randomized, double-blind, placebo controlled, multiple dose study to evaluate the efficacy of AMG 181 in patients with moderate to severe CD is underway. (23) Lastly, Ptg-100, an oral anti-integrin has been shown to achieve high concentrations in intestinal tissue and is being studied for therapeutic potential. (25)

Uncovering real world evidence of existing and available therapies, helps to bring the medical community closer to the goal for treating IBD, which is achievement and maintenance of remission. (3)

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<tr>
<th>Potential learner</th>
<th>Gastroenterologists and other health care professionals (HCP) who treat patients with ulcerative colitis</th>
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<tr>
<td>Educational format</td>
<td>1) Live symposium at CCFA 2016 with an enduring component. 2) Other educational initiatives including delivery formats and learning techniques based on adult learning principles and tailored to independently identified gaps of the learners will be considered.</td>
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<td>Outcome measures</td>
<td>At minimum, the educational evaluation plan must be designed to objectively measure improvements in HCP knowledge and competence (Level 4) (15).</td>
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<td>Funding guide</td>
<td>Budget should demonstrate fiscal responsibility and cost effectiveness.</td>
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<td>Submission Requirements</td>
<td>When responding to this CGA, please follow the established guidelines for the Takeda medical education grant submission process. If the activity includes multiple providers the accredited provider must submit the grant request. All applications must be submitted online through <a href="http://www.takedaeducationalgrants.com">www.takedaeducationalgrants.com</a>. Grant applications submitted after the deadline will not be reviewed. The education must be accredited by the appropriate accrediting bodies, be fully compliant with ACCME criteria and the Standards for Commercial Support and must be in accordance with the U.S. Food and Drug Administration’s Guidance on Industry-Supported Scientific and Educational Activities. If accepted, must attest to the terms, conditions and purposes of an educational grant as described in the Takeda letter of agreement.</td>
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Immediately upon reconciliation, Takeda will solely determine if Provider or any Educational Partner made any value transfers in connection with the educational activity that must be reported in connection with Commercial Interest’s Transparency Reporting program. Should Takeda determine that a particular value exchange must be reported, Provider and/or Educational Partner shall provide any information requested by Takeda within thirty (30) days of the request. Provider and Educational Partners shall not withhold any information reasonably required by Commercial Interest in connection with its reporting obligations.

References


3. Gordon, Jason P.a.e; McEwan, Phil Ca,b; Maguire, Andy;c Sugrue, Daniel Ma; Puelles, Jordeg. Characterizing unmet medical need and the potential role of new biologic treatment options in patients with ulcerative colitis and Crohn’s disease: a systematic review and dinidian surveys. European Journal of Gastroenterology & Hepatology Issue: Volume 27(7), July 2015, p 604–812


