

Thursday, March 19, 2020

Dear Investigator,

Bristol Myers Squibb (BMS) is rapidly responding to the arising challenges in relation to coronavirus (COVID-19) and the effect this is having on the conduct of clinical trials.

Like you, we are closely monitoring the evolving situation across the globe, and we are taking proactive steps to protect the safety of study participants, our employees and staff at our clinical trial sites while also ensuring regulatory compliance and the scientific integrity of trial data. We are also taking into consideration that your time and your clinic's resources may need to be re-directed in support of the broader community during this time.

To this end, R&D leaders at BMS have developed overarching principles and guidance for the conduct of BMS clinical research in light of COVID-19; in addition, several health authorities have provided guidance for conduct of clinical trials at this time. Based on these, we have aligned on some key decisions of which we would like to make you aware. These decisions pertain to trials executed by BMS directly or through a Contract Research Organization (CRO) and include the following:

**Ongoing Studies - those that have passed global First Patient First Visit (FPFV)**

- **New Patient Enrollment** - Sites may continue to recruit new patients into ongoing trials if:
    - We have confirmation that sites are able to recruit and manage those new patients effectively and in compliance with the protocol; and
    - We either have access to the site to perform on-site monitoring of data or there are existing, established processes with a site for direct access to the Electronic Medical Record (EMR).
  - **Site Monitoring** - We will utilize all mechanisms to be in contact with you to ensure we support you and your team at this time. We understand that, at some sites, on-site monitoring visits are not feasible. In these cases, we will leverage remote monitoring tactics to review data for ongoing patients.
  - **Site Activation** - New site activations for ongoing studies will be suspended as of close of business on March 20 through April 13, 2020. This timeframe could extend beyond April 13, and we will follow up with further direction if that becomes the case. Any site initiations during the week of March 16 will continue as planned as long as the BMS or CRO staff have on-site access.
  - **Patient Site Visits** - For ongoing patients who are unable or unwilling to attend protocol-specified trial visits and procedures, they will remain in the trial for as long as you deem appropriate and for as long as the patient continues to consent to participation.
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**New Studies - those yet to achieve global FPFV**

- **Site Activation** - Effective immediately, we will not initiate or activate any sites globally for new studies until April 13, 2020. This timeframe could extend beyond April 13, and we will follow up with further direction if that becomes the case. We will also not perform further retraining or refresher visits during this time for sites that are not actively treating participants in a trial.

**Studies Involving Healthy Volunteers (HV)**

- Studies involving HV should not initiate and new sites should not be activated until April 13, 2020. If the HV study has not begun enrolling (i.e. in screening, but not yet reached FPFV) it should be paused until April 13, 2020, at a minimum. If the HV study is at a natural break point (e.g. in between cohorts, between study parts, etc.), it should be paused until April 13, 2020, at a minimum. All recommendations for BMS studies, ethics committees, local health authorities and central health authorities should be followed.

**Suspected/Confirmed COVID-19**

- **New Participant Enrollment** - For participants who are exhibiting symptoms consistent with COVID-19 or have tested positive using a test consistent with the institutional standard of care, enrollment and protocol treatment should not be initiated until resolution of symptoms and evaluation by you.
- **Ongoing Participant Treatment** - For participants who are exhibiting symptoms consistent with COVID-19, you should hold dosing of investigational product, and we ask that you consult the Medical Monitor. In the event a participant tests positive for COVID-19, or if no testing is available, you should hold dosing until such time as symptoms resolve. If a positive COVID-19 test result is reported, please consult with the Medical Monitor on whether resolution of symptoms alone without retesting is sufficient to resume dosing of the investigational product.

**Further Considerations Across Studies**

You should weigh the public health considerations and individual benefit-risk in enrollment and treatment decisions for trial participants during the COVID-19 pandemic.

You should carefully consider the impact of any travel restrictions implemented by local/regional health authorities and local institutions on the benefit-risk in enrollment and treatment decisions.

**Investigator-Sponsored Research (ISR)/Investigator-Initiated Trials (IIT)**

- BMS internal company operations related to the support of ISRs and IITs are functioning without interruption. Therefore, necessary activities needed for the continued progress of ISR/IITs, such as site activation, drug supply and site payment, will continue as normal. Additionally, we will not change our internal procedures related to the review of newly proposed concepts.
- We understand that each institution will deploy specific COVID-19 guidance to follow as it pertains to your ISR/IIT clinical trial practice(s). We anticipate this may have

an impact on study activities, including site activation and enrollment of your study participants. We will continue to collaborate with you to adjust timelines and enrollment plans as needed throughout this period of uncertainty, ensuring patients have safe access to participate in trials while adhering to local policies and processes instituted in light of the COVID-19 pandemic.

In addition to the above, BMS R&D leaders are continuing to evaluate recommendations related to:

- safety, including interruption of dosing, enrollment, monitoring and treatment discontinuation/interruption
- ensuring compliance with essential ICH/GCP requirements - we continue to monitor emerging Health Authority guidance and IRB recommendations
- ensuring the scientific integrity of clinical research in areas of potential impact such as collection and interpretation of key data needed because of treatment interruptions, missing data and adverse events

We will also be in touch with further guidance as studies approach database lock.

We recognize this is a rapidly evolving situation and we will continue to provide timely updated guidance related to BMS clinical research. This includes, in some cases, additional guidance and actions for your specific trial(s).

Please reach out to your BMS Study Team with any questions and as you become aware of new information that would impact your ability to safely treat patients in any of our studies. Please also ensure this communication is filed in your study file and notify your IRB/Ethics Committee, as applicable, based on your institution's policy. We will inform Health Authorities of our decisions in accordance with local regulations.

As a reminder, you may also contact the BMS Medical Information line in your region for customer service, patient assistance information, product information and adverse event reporting. You can find the local contact information at [www.globalbmsmedinfo.com](http://www.globalbmsmedinfo.com)

Thank you for your partnership in our shared mission of caring for patients and our communities, and for all you're doing on the frontlines of this pandemic. We have confidence that, together, we all will effectively manage through this very challenging situation.

Regards,

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