BALVERSA™ (erdafitinib) Diagnostic *FGFR* Genetic Testing – Specimen Requirements and Shipping Guidelines

Role of *FGFR* gene testing in bladder cancer:

Mutations in fibroblast growth factor receptors (*FGFRs)* have been shown to play a role in bladder cancer, and is linked to tumor growth, metastasis and overall prognosis. BALVERSA™ (erdafitinib) is a kinase inhibitor that binds to and inhibits *FGFR* enzymatic activity. It is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC), whose tumours have susceptible *FGFR2* or *FGFR3* genetic alterations and who have disease progression during or following at least one line of prior chemotherapy, including within 12 months of neoadjuvant or adjuvant chemotherapy.

At this time, two laboratories in Canada will be offering *FGFR* testing to identify patients eligible for treatment with *FGFR* inhibitors. The two sites are: (1) **Genome Diagnostics, UHN, Toronto** (testing site for the provinces of Ontario, Alberta, Manitoba and Newfoundland) and **(2) Molecular Pathology Center, CUISSS Centre-Ouest/Jewish General Hospital, Montreal** (for Quebec, British Columbia, Saskatchewan, New Brunswick, Nova Scotia, Prince Edward Island). Please refer to the **shipping details at the end of this document.**

***FGFR* testing and reporting:**

Testing is performed using a pan-cancer NGS panel which analyzes both DNA and RNA and can detect sequence changes as well as rearrangements involving *FGFR1*, *FGFR2*, *FGFR3* and *FGFR4*. The clinical trials had enrolled UC patients with pre-specified *FGFR* alterations: any of the following ***FGFR* missense mutations (p.Arg248Cys, p.Ser249Cys, p.Gly370Cys, p.Tyr373Cys)** or ***FGFR2/3* gene fusions (*FGFR3-TACC3, FGFR3- BAIAP2L1, FGFR2-BICC1, FGFR2-CASP7***).

- In the current testing offered by the two referral sites, clinically actionable *FGFR* mutations other than those listed above will be also reported, using a somatic variant scheme [PMID: 25880439]
- However, please note that there is no data on the performance of erdafitinib on variants other than the pre-specified ones listed above
- Annotation will be performed using the following resources: (1) somatic variant databases; (2) functional prediction algorithms to determine impact on protein structure and/or function; (3) available medical literature; and (4) data on actionability

Specimen Requirements:

- When possible, the FFPE block is preferred; a ~3mm area will be cored from the block. If a block cannot be sent, please send tissue sections on uncoated air-dried slides shipped at room temperature (8 unstained sections at 7μm). For small biopsies, please contact the laboratory for instructions. For core biopsies, the entire block is required.
- Tumour cellularity must be ≥ 20% tumor cells for accurate test results
- EXTERNAL pathology review and corresponding circled H&E slide required prior to sending block
- For all tissue sections, we require 2 H&E stained sections, one cut before cutting slides from the block and one cut after serial sectioning
- Please note that for transurethral resection of bladder tumour (TURBT) specimens, it is the deep/ invasive part of the tumor rather than the superficial layer that should be tested [PMID: 27091807]
- PLEASE NOTE: **tumour cellularity must be indicated on the requisition**

Shipping Requirements:
Samples should be appropriately labelled and shipped according to these instructions:

- The slides must be shipped to reach the laboratory immediately after sectioning, preferably in an airtight container
- Each slide must be labelled with the patient's name, date of birth and MRN#
- Complete the site-specific clinical requisition form
- Place the slides in an appropriate protective package
- Insert the package in a biohazard plastic bag
- Place the biohazard bag, and completed requisition, into an appropriate outer container for shipping and label the outer container with a biohazard label
- Send to the following address using appropriate methods (FedEx, courier or similar):

All Specimens That DO NOT MEET the above specimen and shipping requirements will be REJECTED.

Testing laboratory for provinces of Ontario, Alberta, Manitoba, Newfoundland: Genome Diagnostics, UHN, Toronto

Webinar on *FGFR* Testing at the UHN and JGH**:** https://www.youtube.com/watch?v=YSR4zS5MhAA

Complete the current Cytogenetics and Molecular Diagnostics requisition form available at:
https://www.uhn.ca/LMP/Pages/services_physicians.aspx

Shipping Address:

Genome Diagnostics, Department of Clinical Laboratory Genetics
Toronto General Hospital
Eaton Wing 11th floor, Room 11-444
200 Elizabeth Street
Toronto, Ontario, M5G 2C4
Phone: (416) 340-4800 ext. 5170