further study in dedicated randomised trials. Finally, the biological mechanisms underpinning potential platinum sensitivity in prostate cancers undergoing lineage plasticity are unclear and require further study. It is also unknown whether platinum treatment reverses lineage plasticity after it has occurred, and whether this might sensitise these cancers to androgen receptor-directed therapies again.

Optimal management of aggressive variant prostate cancer represents an unmet medical need, and new clinical trials specifically addressing this entity are clearly indicated. This study adds to the body of evidence suggesting that such patients need to be managed differently. A randomised phase 3 trial testing the platinum–taxane combination in patients with metastatic castration-resistant prostate cancer and molecularly defined aggressive variant prostate cancer is planned.

Emmanuel S Antonarakis
Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD 21287, USA
eantona1@jhmi.edu

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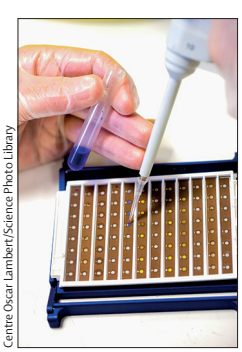
A new screening tool for FGFR inhibitor treatment?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Major advances in targeted therapy and immunotherapy has revolutionised the treatment of cancer. With the advent of personalised medicine, a one-size-fits-all approach is no longer appropriate.[1] Our aim to personalise cancer treatment based on the molecular landscape of tumours has led to development of biomarker-driven strategies to improve treatment outcomes.

The mammalian FGFR family consists of four tyrosine kinase receptors (FGFR1–4) with 22 distinct ligands identified to date.[2] Activation of FGFR results in receptor dimerisation, transphosphorylation of receptor kinase domains, and activation of downstream RAS–MAPK, PI3K–AKT, and STAT signalling pathways. FGFR signalling is involved in cellular proliferation, differentiation, and migration, thus aberrant activation of the pathway due to FGFR amplification, mutations, or gene fusions has been implicated in pathogenesis of several cancers, such as *FGFR3* mutation in urothelial carcinoma.[3] Considering the fact that FGFR is a potential therapeutic target, several non-selective FGFR tyrosine kinase inhibitors such as dovitinib and lenvatinib have been investigated. In March, 2015, lenvatinib was approved by the US Food and Drug Administration for metastatic, radioactive iodine-refractory differentiated thyroid carcinoma.[4] Since non-selective FGFR tyrosine kinase inhibitors target other related receptors such as vascular endothelial growth factor receptors and platelet-derived growth factor receptors in addition to FGFRs, their use is limited by the occurrence of off-target side-effects that result in cardiovascular and liver toxicities.[2,5] This limitation led to the development of selective FGFR tyrosine kinase inhibitors—ie, FGFR1–3 inhibitors, FGFR4 inhibitors, and pan-FGFR inhibitors. In general, selective FGFR inhibitors have a favourable safety profile. On April 12, 2019, erdafitinib was approved by the US Food and Drug Administration for patients with locally advanced or metastatic urothelial carcinoma with susceptible *FGFR3* or *FGFR2* genetic alterations who had progressed on platinum-based

chemotherapy.[6] Despite these successes, the clinical benefit of FGFR inhibitors is limited by the emergence of acquired resistance due to activation of downstream signalling pathways.[7]

The identification of patients who are likely to benefit from FGFR inhibition remains an overarching challenge. Considering the fact that the prevalence of FGFR molecular alterations is low in solid tumours, and responses to FGFR inhibitors have been modest,[2] the utility of FGFR alterations as a biomarker of response must be re-evaluated. In *The Lancet Oncology*, Martin Schuler and colleagues[8] report that compared with screening for FGFR molecular alterations, *FGFR* mRNA-based screening detects a broader patient population eligible for treatment with rogaratinib, a selective pan-FGFR inhibitor. In their study, 866 biopsies from patients with advanced cancer were screened for *FGFR* mRNA expression levels, of whom 126 were treated with rogaratinib (23 patients unselected for *FGFR* mRNA expression and 103 with overexpression of *FGFR* mRNA). The drug showed particularly notable anti-tumour activity in patients with urothelial carcinoma (12 [24%] of 51 evaluable patients with urothelial carcinoma achieved an objective response). The drug had a manageable safety profile. Hyperphosphatemia was the most common adverse event, which is consistent with that reported for other FGFR inhibitors.[9]

The authors made several important observations. First, objective responses were observed in patients with *FGFR* mRNA-overexpressing tumours without apparent FGFR genetic aberration. Responses were similar in patients with and without *FGFR* mutations, suggesting that *FGFR* mRNA rather than *FGFR* alteration might widen the target population who are eligible for treatment with rogaratinib. Second, in patients with urothelial carcinoma, *PIK3CA* or *RAS* gene mutations were identified in 29% of patients who had disease progression, whereas no mutations were identified in patients with an objective response, suggesting that patients with additional molecular alterations in downstream signalling pathways might benefit from combination therapy. Third, objective responses were recorded in patients who had no substantial clinical benefit with previous checkpoint inhibitor treatment, which might be due to FGFR inhibitor-induced reduction or the disappearance of myeloid-derived suppressor cells from the tumour microenvironment.[10]

Where do we go from here? Based on the findings of Schuler and colleagues,[8] the use of *FGFR* mRNA as a biomarker of response to FGFR inhibitors requires validation in a larger cohort. Furthermore, the presence of molecular alterations in downstream signalling pathways should be considered for patient selection. Excluding patients with molecular alterations in pathways known to confer drug resistance from receiving monotherapy has two benefits; the proportion of patients achieving a response with FGFR inhibitors might increase, and more importantly, these patients could be treated with FGFR inhibitor-based combination therapy to overcome acquired resistance. Since combination therapies are associated with an increased risk of toxicity, these studies should be done on the basis of strong preclinical data and high risk–benefit ratios. Schuler and colleagues[8] observed objective responses among patients with solid tumour types other than urothelial carcinoma, thus the efficacy of rogaratinib in other FGFR mRNA-expressing tumours must be explored. Hyperphosphataemia is an on-target effect of specific FGFR inhibitors; therefore, the role of elevated serum phosphate concentrations as a surrogate marker of response to treatment warrants evaluation. By incorporating the rapidly evolving data from translational studies into clinical practice, FGFR inhibitors might be a promising treatment strategy for patients with FGFR-dependent cancers.

Aung Naing
Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
anaing@mdanderson.org

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Improving care for the overlooked in oncology: incarcerated patients

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Physicians and public health practitioners often view health disparities through the eyes of birthplace, race, sex, economic class, sexuality, religion, or neighbourhood, or a combination of these. In the process, patients who are incarcerated (too often referred to as prisoners rather than patients)[1] are overlooked as a profoundly medically vulnerable population with substantial disparities in health care and their health is an understudied public health crisis.[2] Although a third of illness-related deaths in US state prisons are due to cancer, and this mortality rate is double for incarcerated male patients,[3] few recommendations exist to guide oncologists in how to address the unique challenges of providing ethically competent and high quality cancer care for incarcerated patients.

Adults who are incarcerated in the USA comprise approximately 1% of the total adult population and about 20% of approximately 10 million individuals who are incarcerated worldwide.[4] The proportion of people who are incarcerated and aged 55 years or older is expected to reach a third of the total prison population in the USA, an estimated 400 000, by 2030.[4] Yet, little data exist on patients who are incarcerated among the studies of cancer health disparities,[5] and the few studies that do exist show unequal access to cancer screening, both during and before incarceration.[6] These inequities can have a profound effect on community health because most people who are incarcerated will eventually return to communities where they will rely on public health systems for health care, including cancer care. As a result, a dire need exists for policy makers and health-care practitioners to collaborate on initiatives that improve the health of patients who are incarcerated.

In oncology, which relies on a multidisciplinary approach and intimate physician–patient relationships, patients who are currently incarcerated might be more vulnerable than others. For example, some incarcerated individuals—disproportionately of racial or ethnic minorities—might have a past experience of racial or ethnic prejudice in the health-care system, while others might have physical or emotional trauma. For these patients, building trust and maintaining a relationship with a health provider can be more challenging,[7,8] and so building trust in the physician–patient relationship might require culturally sensitive exploration of previous psychosocial trauma, including previous incarceration.

The lack of knowledge about the health and health-care needs of individuals who are incarcerated, including the best ways to treat those with serious or life-threatening illnesses such as cancer,[9] can exacerbate patients' suspicions of injustice and restricts clinicians' knowledge of the best ways to approach this medically and socially complex patient population. Therefore, we have developed a framework (panel) to guide the approach to cancer care in this population.

First, collection of data and development of measures to understand the quality of oncological care provided to incarcerated patients across correctional facilities and jurisdictions, the ways that this care differs from that of the community, and opportunities for improvement and optimisation is essential. Such data collection should follow a principled approach designed to track outcomes and appropriately identify areas for intervention.[10]

Second, an oncology task force is needed to identify any disparity in patients who are incarcerated in prevention, assessment, and treatment of cancer. Such a taskforce could, at a minimum, encourage the US national cancer database, a registry with more than 70%