> Such a 'time-limited therapy' paradigm is only made potentially feasible by the high rate of MRD negativity

serious adverse event observed in early trials of venetoclax, was only 3.1%. These findings "definitely establish the safe deliverability of the agent with the now well documented and widely known weekly dose ramp-up schedule, TLS prophylaxis and monitoring, and 'risk-adapted' selective inpatient admission of a minority of patients," says Seymour.

In the MURANO study, venetoclax treatment is being withdrawn after 2 years. "Such a 'time-limited therapy' paradigm is only made potentially feasible by the high rate of MRD negativity," Seymour explains. This approach might decrease the risk of acquired drug resistance, reduce morbidity, improve treatment adherence, and provide economic benefits. "Longer follow-up study of the patients from the MURANO trial after drug cessation has the potential to establish this paradigm as a standard approach," Seymour concludes.

David Killock

ORIGINAL ARTICLE Seymour, J. F. et al. Venetoclax–rituximab in relapsed or refractory chronic lymphocytic leukemia. *N. Engl. J. Med.* **378**, 1107–1120 (2018)

Credit: Science History Images/Alamy

previous data indicating that, similar to vemurafeib, the combination of encorafenib with a MEK inhibitor enabled a higher dose of the BRAF inhibitor to be delivered.

Notably, encorafenib alone provided a small, albeit not statistically significant, improvement in PFS duration compared with vemurafenib, presumably owing to the ability to target a broader range of mutant BRAF proteins and/or the considerably longer dissociation half-life of this agent.

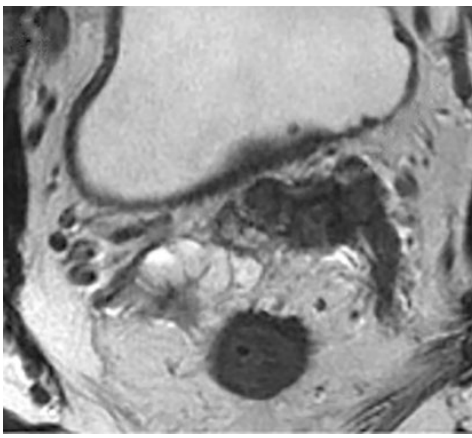
Overall, the PFS outcomes from the COLUMBUS trial suggest that encorafenib is a viable alternative to vemurafenib; however, overall survival outcomes are eagerly awaited, as are trials comparing encorafenib–binimetinib with other BRAF–MEK inhibitor combinations.

Peter Sidaway

ORIGINAL ARTICLE Dummer, R. *et al.* Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol.* https://doi.org/10.1016/S1470-2045(18)30142-6 (2018)

PROSTATE CANCER

MRI improves diagnosis



Credit: Bjurlin, M. A. et al. *Nat. Rev. Urol.* 12, 617–628 (2015)

Men with a suspicion of prostate cancer, owing to a high serum prostate-specific antigen (PSA) level or other features, routinely undergo transrectal ultrasonography (TRUS)-guided biopsy sampling; however, this approach might not provide the most accurate diagnosis. Now, the findings of a randomized controlled trial demonstrate the superiority of MRI-targeted over TRUS-guided biopsy sampling in men with suspected prostate cancer.

Lead author Veeru Kasivisvanathan explains: "Emerging reports in the literature suggested that using an alternative diagnostic pathway, MRI and MRI-targeted biopsy, showed promising prostate cancer detection rates." Therefore, "in 2012, we set out in an international working group to design a study that could change clinical practice and replace the standard of care with a pathway involving MRI."

A total of 500 men with a suspicion of prostate cancer were randomly assigned to undergo multiparametric MRI followed by targeted biopsy sampling of a maximum of three specific regions, or standard TRUS-guided biopsy sampling. The proportion of men with clinically significant prostate cancer (summed Gleason score of ≥7) was the primary outcome.

Clinically significant prostate cancer was detected in a total of 95 men (38%) in the MRI-targeted biopsy group, versus 64 (26%) in the TRUS biopsy group (adjusted difference, 12%, 95% CI 4–20%; $P = 0.005$). Furthermore, fewer patients in the MRI-targeted biopsy group received a diagnosis of clinically insignificant prostate cancer (23 (9%) versus 55 (22%), adjusted difference −13%, 95% CI −19 to −7; $P < 0.001$). No histological evidence of prostate cancer was detected in samples from the four men who underwent biopsy sampling despite no signs of prostate cancer on MRI imaging. These observations, combined with the lack of findings suggestive of prostate cancer in 71 men in the MRI-targeted biopsy group, which enabled these men to avoid biopsy sampling, demonstrate the superiority of MRI-targeted biopsy sampling over the standard-of-care approach.

Limitations of this result include only moderate levels of agreement (78%) between site-specific and central radiologists; although, similar levels of disagreement were observed in the interpretation of samples from either group. The investigators noted that the risk of failing to detect clinically significant prostate cancer using MRI-targeted biopsy sampling in other studies is generally low (0–10%); although direct comparisons of the performance of both diagnostic pathways in the same patient would likely be prone to bias.

Commenting on the outcomes of this trial, Kasivisvanathan highlights "This trial provides evidence for replacing the current standard-of- care TRUS biopsy pathway with a pathway involving MRI before biopsy sampling." On the future clinical implementation of this approach, in light of the median of 300 MRIs per year reported by radiologists in this trial, Kasivisvanathan adds "clinicians should be educated on prostate MRI in order to deliver high-quality MRI results that are also accurately reported". Despite these promising results, investments in terms of both increased capacity for MRI and greater levels of training would need to be made available if this improved diagnostic pathway is to be universally adopted.

Peter Sidaway

ORIGINAL ARTICLE Kasivisvanathan, V. *et al.* MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1801993 (2018)