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- Aldape, K. et al. Challenges to curing primary brain tumours. Nat. Rev. Clin. Oncol. https://doi.org/10.1038/ s41571-019-0177-5 (2019).
- Michalski, J. M. et al. Results of COG ACNS0331: a phase III trial of involved-field radiotherapy (IFRT) and low dose craniospinal irradiation (LD-CSI) with chemotherapy in average-risk medulloblastoma: a report from the Children's Oncology Group. Int. J. Radiat. Oncol. Biol. Phys. 96, 937–938 (2016).
- Bailey, C. C. et al. Prospective randomised trial of chemotherapy given before radiotherapy in childhood medulloblastoma. International Society of Paediatric Oncology (SIOP) and the (German) Society of Paediatric Oncology (GPO): SIOP II. Med. Pediatr. Oncol. 25, 166–178 (1995).
- Walker, M. D. et al. Evaluation of BCNU and/or radiotherapy in the treatment of anaplastic gliomas. A cooperative clinical trial. J. Neurosurg. 49, 333–343 (1978).

- Laperriere, N. et al. Radiotherapy for newly diagnosed malignant glioma in adults: a systematic review. *Radiother. Oncol.* 64, 259–273 (2002).
- Balmaceda, C. et al. Chemotherapy without irradiation

   a novel approach for newly diagnosed CNS germ cell tumors: results of an international cooperative trial.

   The first international central nervous system germ cell tumor study. J. Clin. Oncol. 14, 2908–2915 (1996).
- Rogers, S. J., Mosleh-Shirazi, M. A. & Saran, F. H. Radiotherapy of localised intracranial germinoma: time to sever historical ties? *Lancet Oncol.* 6, 509–519 (2005)
- Merchant, T. E. et al. Conformal radiation therapy for pediatric ependymoma, chemotherapy for incompletely resected ependymoma, and observation for completely resected, supratentorial ependymoma. J. Clin. Oncol. 37, 974–983 (2019).
- Chang, E. L. et al. (eds) Adult CNS Radiation Oncology 1st edn (Springer, 2018).
- Ludmir, E. B. et al. Increased risk of pseudoprogression among pediatric low-grade glioma patients treated with

- proton versus photon radiotherapy. *Neuro-oncology* **21**. 686–695 (2019).
- Gilbo, P., Zhang, I. & Knisely, J. Stereotactic radiosurgery of the brain: a review of common indications. *Chin. Clin. Oncol.* 6 (Suppl. 2), S14 (2017).
- Ladra, M. M., MacDonald, S. M. & Terezakis, S. A. Proton therapy for central nervous system tumors in children. *Pediatr. Blood Cancer.* 65, e27046 (2018).
- Indelicato, D. J. et al. Consensus report from the Stockholm Pediatric Proton Therapy Conference. Int. J. Radiat. Oncol. Biol. Phys. 96, 387–392 (2016).
- Bindra, R. S. et al. GBM radiosensitizers: dead in the water... or just the beginning? *J. Neurooncol.* 134, 513–521 (2017).
- US National Library of Medicine. ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/record/NCT01878617 (2019)

### **Competing interests**

The authors declare no competing interests.

# Reply to 'Assembling the brain trust: the multidisciplinary imperative in neuro-oncology'

Kenneth Aldape, Kevin M. Brindle, Louis Chesler, Rajesh Chopra, Amar Gajjar, Mark R. Gilbert, Nicholas Gottardo, David H. Gutmann, Darren Hargrave, Eric C. Holland, David T. W. Jones, Johanna A. Joyce, Pamela Kearns, Mark W. Kieran, Ingo K. Mellinghoff, Melinda Merchant, Stefan M. Pfister, Steven M. Pollard, Vijay Ramaswamy, Jeremy N. Rich, Giles W. Robinson, David H. Rowitch, John H. Sampson, Michael D. Taylor, Paul Workman and Richard J. Gilbertson

We thank Ludmir and colleagues (Ludmir, E. B. et al. Assembling the brain trust: the multidisciplinary imperative in neuro-oncology. Nat. Rev. Clin. Oncol. https://doi.org/10.1038/ s41571-019-0235-z (2019))1 for their positive comments on our Position Paper (Aldape, K. et al. Challenges to curing primary brain tumours. Nat. Rev. Clin. Oncol. https://doi. org/10.1038/s41571-019-0177-5 (2019))2, and we agree entirely that radiation oncology has, and will likely continue to have for many years, a critical role in the treatment of patients with primary brain tumours. In particular, we note the helpful references to newer radiotherapy approaches, such as stereotactic radiosurgery and proton beam therapy, that are advancing the treatment of brain tumours. As noted by Ludmir and colleagues1, a substantial portion of our Position Paper<sup>2</sup> is given over to the discussion of radiation oncology.

As stated in our manuscript<sup>2</sup>, this narrative was composed following a series of international, multidisciplinary meetings, hosted by Cancer Research UK, which engaged many individuals involved in brain tumour research and treatment. It is important to note that our manuscript is a Position Paper and not a Meeting Report. Thus, rather than

synthesising the entirety of the discussions that took place during these meetings, it reports the opinions of those authors listed on the paper. The discussions held by the committee did indeed engage radiation oncologists as well as individuals in other disciplines; however, other commitments precluded these individuals from participating in many of the meetings and in the writing of our Position Paper<sup>2</sup>. Nonetheless, we wish to assure Ludmir and colleagues<sup>1</sup> that the entire brain tumour research and treatment community recognizes and values the importance and contribution of radiation oncology to the management of brain tumours. We very much look forward to continuing our interactions with colleagues in this discipline for the good of all patients with these terrible diseases.

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- Ludmir, E. B. et al. Assembling the brain trust: the multidisciplinary imperative in neuro-oncology. *Nat. Rev. Clin. Oncol.* https://doi.org/10.1038/10.1038/ s41571-019-0235-z (2019).
- Aldape, K. et al. Challenges to curing primary brain tumours. Nat. Rev. Clin. Oncol. https://doi.org/10.1038/ s41571-019-0177-5 (2019).

## Competing interests

P.W. and R.C. are employees of The Institute of Cancer Research (ICR), which has a commercial interest in a range of drug targets. The ICR operates a Rewards to Inventors scheme whereby employees of the ICR may receive financial benefit following commercial licensing of a project. P.W. is a consultant and/or scientific advisory board member for Nextechlnvest, Storm Therapeutics, Astex Pharmaceuticals and CV6 and holds stock in Chroma Therapeutics, NextInvest and Storm Therapeutics; he is also a Non-Executive Director of Storm Therapeutics and the Royal Marsden NHS Trust and a Director of the non-profit Chemical Probes Portal. R.C. is an adviser to Syncona Limited and holds equity in Celgene Corporation, e-Therapeutics and Monte Rosa Therapeutics. The other authors declare no competing interests.