Comment: Intra-arterial chemotherapy for retinoblastoma

We congratulate the authors on an expounded study on intra-arterial chemotherapy (IAC) for retinoblastoma (RB) published in your esteemed journal. Although the authors write an illustrative series, we believe that there are certain questions unanswered on the topic.

In the handful of studies on IAC for RB, the rate of successful catheterization reported is 98%. Did the authors ever find the ophthalmic artery inappropriate for selective catheterization? What were the alternative routes taken if the ophthalmic artery was not fully developed, or if the access from the internal carotid artery was too acute?

Did the authors document the visual acuity or encounter any case of foveal/choroidal atrophy? Long-term visual outcomes after intravenous chemotherapy (IVC) are well known, but despite the efficacy of the IAC; we are yet unaware of its visual outcomes. Could the potentially high dose of focused chemotherapy be causing more ischemic complications leading to an overall poor visual outcome despite a globe salvage?

The protocols followed for advanced RB are imprecise, largely influenced by personal choice and technical resources. Since the patients received 1–11 cycles of IVC, the indications of IAC are not reflected from the study. Only two cases treated by authors were unilateral, but we should remember that unilateral nongermline advanced diseases are best treated by IAC. Furthermore, the authors were unable to compare the outcomes of primary and secondary IAC due to smaller numbers.

Successfully running a separate RB clinic for the past 20 years, we share our experience in IAC for RB in Table 1. Although literature does not address this issue, three patients developed new lesions after IAC in our series.

### Table 1: Details of patients receiving intra-arterial chemotherapy

| Case | UL/BL | ICRB group | Primary/secondary | Before IAC | Number of IAC cycles | Drug (mg; Average dose in cases of multiple cycles) | Dose | Regression | RD | Globe salvage yes/no | Recurrence |
|------|-------|------------|------------------|------------|----------------------|---------------------------------------------|------|------------|----|----------------------|------------|
| 1    | U/L E | Primary    | -                | 1          | Melphalan 4          | Reduction in tumour mass (75% - 100%)        | 75%  | 100%       | 100% | Yes                  | No         |
| 2    | B/L D1| Secondary  | VEC × 6          | 1          | Melphalan 4          | Vitreous seeds (75%)                         | 75%  | -          | 100% | No; New lesions       | 6 months after enucleated |
| 3    | B/L B | Secondary  | VEC × 3          | 2          | Melphalan 4          | Subretinal seeds (100%)                      | 100% | -          | 0%  | Yes                  | No         |
| 4    | U/L D3| Primary    | -                | 1          | Melphalan 4.2        | <25%                                        | <25% | 0%         | 0%  | No                   | enucleated |
| 5    | U/L B | Secondary  | VEC × 3          | 2          | Melphalan 4          | Vitreous seeds (75% - 100%)                  | >75% | -          | -   | Yes                  | No         |
| 6    | U/L C1| Secondary  | VEC × 3          | 1          | Melphalan 4          | Vitreous seeds (100% - 100%)                 | 100% | -          | 100% | Yes                  | No         |
| 7    | U/L D1| Primary    | -                | 2          | Melphalan 4.5        | Vitreous seeds (75% - 50% - 100%)            | >75% | -          | 50% | Yes                  | No         |
| 8    | U/L C1| Primary    | -                | 2          | Melphalan 4.5        | Vitreous seeds (100% - 100% - 100%)          | 100% | -          | 100% | Yes                  | No         |
| 9    | B/L D1| Secondary  | VEC × 4          | 2          | Melphalan 5.5        | Vitreous seeds (50% - 100% - 100%)           | >50% | -          | 100% | Yes                  | New lesion |
| 10   | B/L D1| Secondary  | VEC × 2          | 1          | Melphalan 5.5        | Vitreous seeds (75% - 100% - 100%)           | >75% | -          | 100% | Yes                  | No         |
| 11   | U/L B | Secondary  | VEC × 2          | 1          | Melphalan 4          | Vitreous seeds (80% - 80% - 100%)            | >80% | -          | 80%  | Yes                  | New lesion |
| 12   | B/L D2| Secondary  | VEC × 2          | 3          | Melphalan 5 + 0.2, 4 + 0.4 topotecan  | Vitreous seeds (75% - >80% - >80%)           | >75% | >80%       | >80% | Yes                  | No         |

U/L: Unilateral, B/L: Bilateral, IAC: Intra-arterial chemotherapy, VEC: Intravenous chemotherapy consisting of vincristine, etoposide, and carboplatin, RD: Retinal detachment, ICRB: International Classification of Retinoblastoma
We endorse IAC in selective cases of RB but until well-established indications are laid down; we should use this modality with caution.

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Conflicts of interest
There are no conflicts of interest.

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Table 1: Visual outcomes for patients undergoing intra-arterial chemotherapy: 2 years follow-up

| Age at diagnosis (months) | Baseline visual acuity | Final visual acuity |
|--------------------------|------------------------|--------------------|
| 32                       | Fixates and follows    | Not applicable     |
| 8                        | Fixates and follows    | Not applicable     |
| 13                       | Fixates                | Fixates and follows|
| 36                       | CSM                    | 6/30 (Snellen)     |
| 24                       | Fixates and follows    | 6/9.5 at 3m (lea symbols) |
| 16                       | CSM                    | Fixates and follows|
| 48                       | 6/7.5 (lea symbols)    | 6/30 (unaided, lea symbols) |
| 11                       | Fixates and follows    | Fixates            |
| 20                       | No fixates             | CSM                |
| 28                       | CSM                    | 6/15 (lea symbols)  |

CSM: Central, steady, and maintained