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CORRESPONDENCE

Trials without borders—decentralized trials and ensuring access to novel cancer therapies during a global pandemic

We read with great interest the recent review by Sessa et al.[1] detailing the impact of COVID-19 on oncology research. The pandemic necessitated significant changes in cancer clinical trial conduct.[2] Correspondingly, regulatory bodies issued detailed guidance for contingency measures, on remote study visits, delivery of investigational product (IP), and site monitoring visits.[1] Two years on, however, with increasing uptake of vaccinations and lifting of restrictions across regions, many trials may simply return to pre-pandemic standard practices. There is a significant challenge to translate and implement the most cost-effective operational approaches for future trials. To this end, we present a single-centre case study on the impact of COVID-19 on trial conduct in an early phase trials unit in an academic cancer centre demonstrating the feasibility of long-term adaptations incorporating a decentralized trials model.

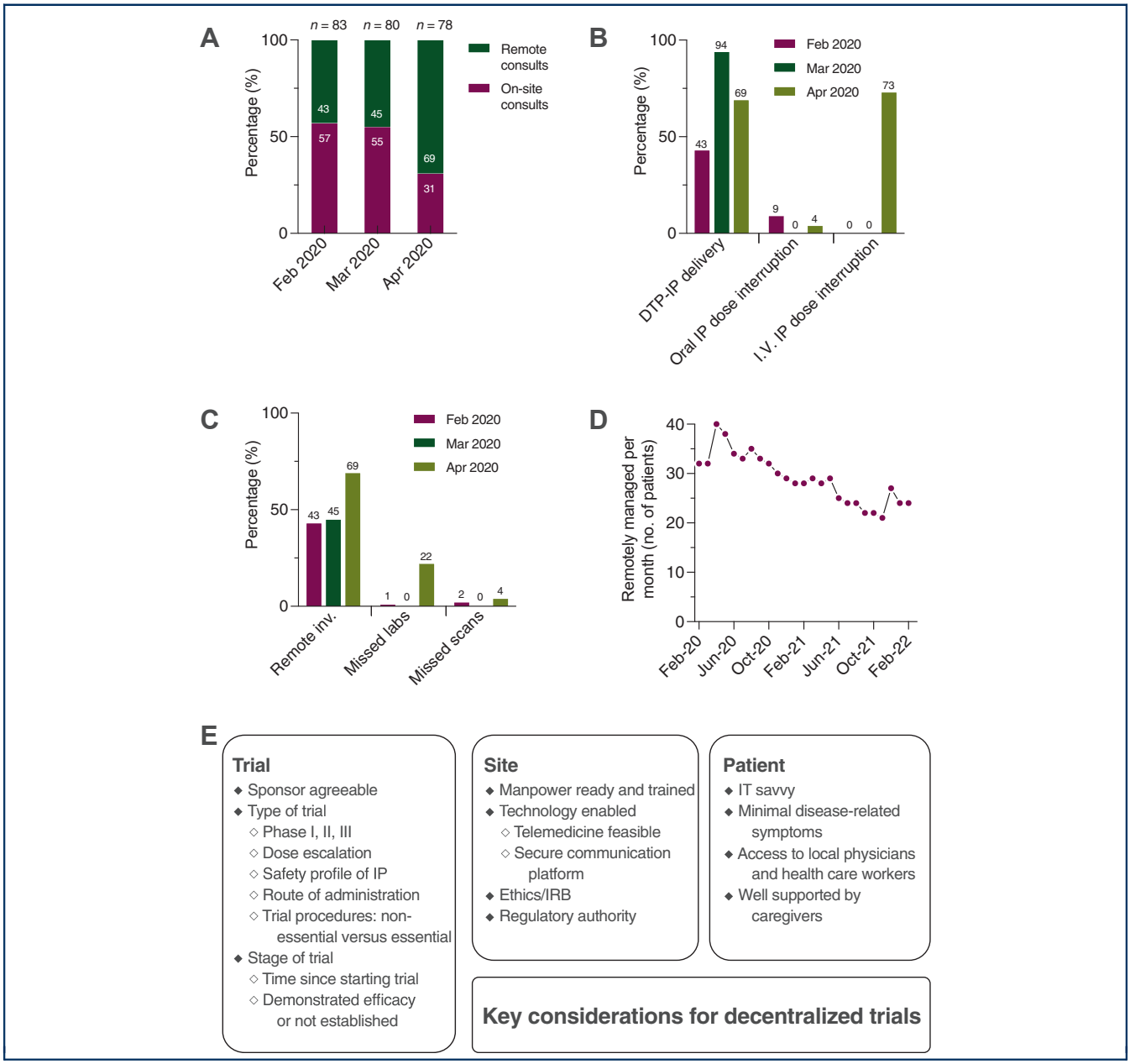

Figure 1. Effect of COVID-19 on trial procedures for ongoing early phase trial patients at the National Cancer Centre Singapore. (A) Remote versus on-site consultations. (B) Treatment continuation for ongoing trial patients. (C) Safety and efficacy assessments for ongoing trial patients. (D) Patients managed remotely per month with remote consultations, investigations, and DTP-IP. (E) Key considerations for decentralized trials.
DTP, direct-to-patient; inv, investigations; IP, investigational product; IRB, institutional review board; I.V., intravenous.

Singapore experienced local community transmission of COVID-19 in early 2020, with restrictions and increased vigilance enforcing rapid changes to routine clinical care.[3] Accordingly, extensive disruptions to trial activities were encountered in the Experimental Cancer Therapeutics Unit (ECRU), Division of Medical Oncology, National Cancer Centre Singapore (NCCS). Notably, this included the extended impact on trial patients residing in neighboring countries throughout Asia (China, Indonesia, Malaysia, Philippines, Sri Lanka, and Vietnam). During the greatest restrictions (February-April 2020), patient consultations were increasingly conducted via remote means (Figure 1A). As patients could not attend sites as per treatment schedules, treatment continuation was impacted, with intravenous treatments most severely affected (Figure 1B). Utilization of direct-to-patient (DTP) delivery, however, including to neighboring countries, mitigated the effect for oral IPs. Similarly, remote investigations allowed for continuity of safety/efficacy evaluations (Figure 1C). Reimbursement processes were established to allow foreign patients to have investigations carried out locally and results and images delivered to NCCS for formal review. As border restrictions remained in place, remote consultations/investigations and DTP-IP delivery have continued (Figure 1D) to allow patients ongoing access to safe and effective novel trial therapies.

The ability to adapt in individual early phase trial units has been previously described across Asia.[4] Some key learning points include the need to triage essential and non-essential activities, continuously re-assess risk/benefit ratios of each trial intervention/procedure, and importantly close dialogue with all stakeholders including patients and ethics boards (Figure 1E). This single-centre experience further illustrates how components of a decentralized trials model can be safely and feasibly implemented, even for international patients on early phase trials. For patients with rare molecular oncogenic drivers, access to effective novel targeted therapies through early phase trials represents a crucial therapeutic avenue. Nevertheless, patient safety remains paramount, and ethical, regulatory, and trial sponsor considerations must be taken into account.[5] Of note, patients in our centre who continued with remote consultations were on oral targeted therapies, and already tolerating and responding to therapy—having commenced treatment and completed initial study visits in-person. Ultimately, therefore, a hybrid model with patient-centric decentralized processes whilst balancing aspects ensuring patient safety, may represent the positive long-lasting impact of the COVID-19 pandemic on cancer clinical trials.

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REFERENCES

1. Sessa C, Cortes J, Conte P, et al. The impact of COVID-19 on cancer care and oncology clinical research: an experts' perspective. *ESMO Open*. 2022;7(1):100339.
2. Tan AC, Ashley DM, Khasraw M. Adapting to a pandemic - conducting oncology trials during the SARS-CoV-2 pandemic. *Clin Cancer Res*. 2020;26(13):3100-3103.
3. Wong JEL, Leo YS, Tan CC. COVID-19 in Singapore-current experience: critical global issues that require attention and action. *JAMA*. 2020;323:1243-1244.
4. Shimizu T, Kim DW, Loong HH, et al. Overcoming the impact of the COVID-19 pandemic on oncology early phase trials and drug development in Asia-Experiences and perspectives of the Asian Oncology Early Phase 1 Consortium. *Asia Pac J Clin Oncol*. 2021;17(4):388-395.
5. Vignot S, Martin M, Albin N, Schurtz C, Chapel E. Facilitating access to new therapeutic options through clinical trials: the vision of a regulator to reconcile innovation and safety. *Ann Oncol*. 2019;30(11):1694-1696.