Evaluating the outcomes of existing processes for drug interactions identified via manual checking for patients on vorasidenib with IDH-mutant grade 2 oligodendrogliomas or astrocytomas

Victoria Bugaj Petrou[1], Susan Singh[1], Nandini Patel[2], Alezeh Allidina[1], Maria Marchese[1,3], Carlo De Angelis[1,3], Christine Peragine[1]

Underlined: presenting & senior author

[1]Odette Cancer Care Centre, Sunnybrook Health Sciences Centre (SHSC); [2]University of Waterloo, School of Pharmacy; [3]University of Toronto, Leslie Dan Faculty of Pharmacy

Scan this QR code to download this poster & other Sunnybrook posters

BACKGROUND/OBJECTIVE

Vorasidenib is the first medication targeting IDH1/IDH2 mutations in patients with grade 2 oligodendrogliomas or astrocytomas to delay the need for further treatment and preserve quality of life. Vorasidenib has high risk of drug-drug interactions (DDIs) as it is an inducer of CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP3A4 and UGT1A4. Vorasidenib was fast tracked under the Priority Review Policy and drug interactions were not available in standard of care tertiary drug interaction software (i.e. Lexicomp). The purpose of this study is to assess whether existing processes are reliable to assess DDIs in a non-conventional manner and to describe the drug interactions identified.

METHODS

- Dispensing data from the pharmacy database was used to identify patients who were started on Vorasidenib between 01-Jun-2024 to 13-Nov-2024.
- A Best Possible Medication History (BPMH) was collected and DDI assessments were completed manually. Pharmacists reviewed pharmacokinetic and pharmacodynamic data available in product monographs and available tertiary drug references. In each case, pharmacists determined appropriate interventions and formulated a care plan with each patient (Figure 1).

METHODS

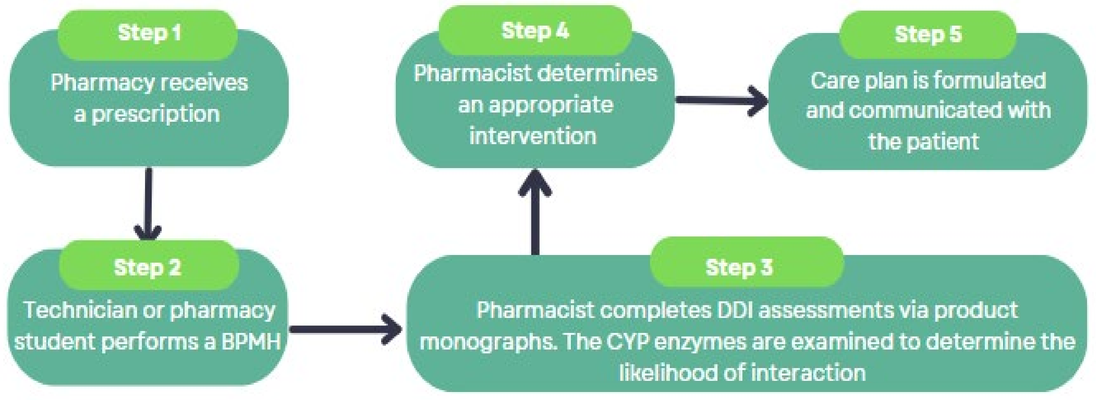

Figure 1: The processes for determining drug interactions for novel anticancer therapy via manual pharmacist assessment

- The rate of BPMHs completed was recorded and the number prescription medications, over-the-counter medications (OCTs), and natural health products (NHPs) used by each patient was noted.
- Counselling history and interventions were extracted from electronic health records.

RESULTS

Drug Category	Total number of monitoring interventions (n=28)	Total number of drug change intervention (n=1)	Total number of drug discontinuation intervention (n=2)	Drug interaction recommendation from Lexicomp
CYP substrate medication (n=22)	21	1*	1	No interaction identified
Cannabis or CBD (n=3)	3	0	0	Level C: Suggestion to monitor therapy if with smoked herb (CYP1A2)
Contraceptiveor hormonal therapy (n=4)	4	0	0	Level D: Consider therapy modification - vorasidenib may decrease serum concentration of hormonal contraceptives
Natural Health Product (n=1), Lion's Mane mushroom	0	0	1	No interaction identified

Table 1: Categorized drugs and their corresponding interventions initiated by pharmacists followed by the ultimate recommendation from Lexicomp.
**There was a single drug incidence (solifenacin) that initially required monitoring and subsequently resulted in a recommendation for therapy change at a later time given a patients' concern for decreased efficacy. Both recommendations were captured as two separate events.*

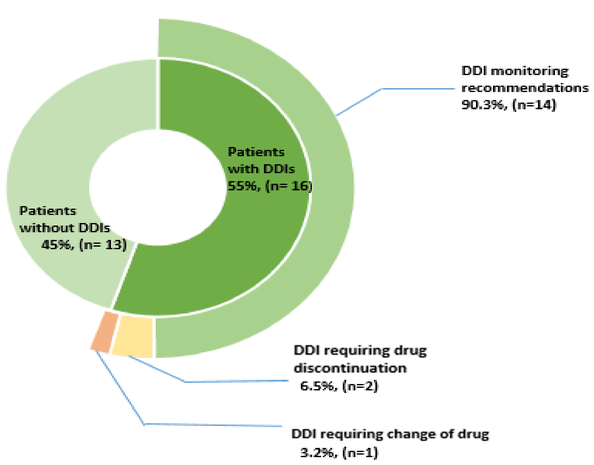

Figure 2: The number of patients (n=29) dispensed vorasidenib with an identified DDI, overlaying total DDIs (n=31) categorized by intervention type.

- Of the 29 patients identified, the median age was 37 years and 55% of the patients were female. Fourteen patients were diagnosed with oligodendrogliomas, and 15 with astrocytomas, all grade 2 IDH mutated.
- The median number of concurrent medications was 2 (n=29, range: 0-9), OTCs was 2 (n=29, range: 0-6) and NHPs was 0 (n=29, range: 0-3). BPMHs were completed for every patient (100%).
- There were 3 instances where a DDI check was missed without a documentation note and one incident where documentation counselling was completed, but DDI assessment was missed. One of the four patients identified to be on hormonal contraceptives did not have the DDI identified at time of counselling.
- Fifty-five percent (n=16) of patients had DDIs with 31 interventions identified in total (Figure 2). Fifty percent of patients (n=8) had more than one DDI.
- With respect to the type of interventions required, majority of the DDIs identified involved the recommendation of monitoring for decreased efficacy due to enzyme induction (n=28). Changes in drug therapy (n=1) and stopping a medication (n=2) were less common. These interventions were compared to the drug interactions identified by Lexicomp once vorasidenib was properly coded in the database (Table 1).

DISCUSSION & CONCLUSION

The rate of BPMHs documented indicates successful processes for obtaining medication history. Presence of missed DDIs highlight need to improve assessment procedures. With high frequency of monitoring interventions, proper follow up is important to ensure therapeutic stability for other comorbid conditions. Notably, there was one intervention which began with monitoring and eventually required a change in drug.

There was also one instance with a missed DDI with a hormonal contraceptive. Given the young demographic and potential for fetal harm with vorasidenib, it is important that DDIs between vorasidenib and hormonal contraceptives are identified and counselled to minimize risk for unplanned pregnancy.

Contrary to what was anticipated, vorasidenib was not coded in databases as a CYP3A4 inducer to CYP3A4 sensitive substrates given lack of evidence describing vorasidenib's potential and magnitude to induce CYP3A4. Our approach was deliberately conservative as to not overlook any clinically significant interactions. This approach reinforces the principle that in evolving drug interaction landscapes, erring on the side of caution is necessary until more definitive data becomes available.

The absence of information does not rule out the potential for vorasidenib to act as a CYP3A4 inducer to sensitive substrates. It is important to counsel patients that recommendations for DDIs can change with time as evidence changes in the context of novel anticancer medications. Equally, the lack of information and DDI flags with Natural Health Products does not necessarily endorse their safety and requires pharmacist assessment and clinical judgement regarding their use.

DDIs for novel anticancer medications are at risk of being missed or improperly assessed and should be dispensed by a pharmacy with experience in oral anticancer medications and enhanced systematic processes.