



## Concomitant Clozapine and Chemotherapy in a Patient with Schizophrenia and Newly Diagnosed Bladder Cancer

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### Introduction

Clozapine is the most effective antipsychotic but comes with potentially life-threatening adverse effects, namely neutropenia.<sup>1</sup>

The majority of chemotherapy treatments cause bone marrow suppression.<sup>2</sup>

This poses a difficult therapeutic dilemma: cease the clozapine and risk a psychotic relapse; or retain clozapine and risk life-threatening neutropenia.

### Objective

To report a case of successful clozapine treatment in a patient undergoing chemotherapy.

### Patient Information

Mr DA, a 59 year old Caucasian male.

Medical history:

- Paranoid schizophrenia
- Bladder cancer (stage T4)
- Type 2 diabetes

Medications:

- Clozapine 250mg nocte
- Escitalopram 30mg mane
- Atorvastatin 80mg nocte
- Metformin 850mg bd
- Fenofibrate 145mg daily
- Ramipril 5mg daily

- Gemcitabine
- Cisplatin
- Dexamethasone
- Metoclopramide
- Oxycodone/naloxone (Targin<sup>®</sup>)

Allergies/Adverse Drug Reactions:

- Nil known

Substance Use:

- THC
- ETOH

### Clozapine Treatment History

- Clozapine commenced in 1994
- Mental state has been stable for approximately 24 years

### Chemotherapy Treatment

eviQ 312 - Bladder/Urothelial locally advanced or metastatic.<sup>3</sup>

Frequency: 21 days<sup>3</sup>

Each cycle:

Gemcitabine 1000mg/m<sup>2</sup> IV infusion on days 1 and 8<sup>3</sup>

Cisplatin 35mg/m<sup>2</sup> IV infusion on days 1 and 8<sup>3</sup>

Four cycles completed at time of writing.

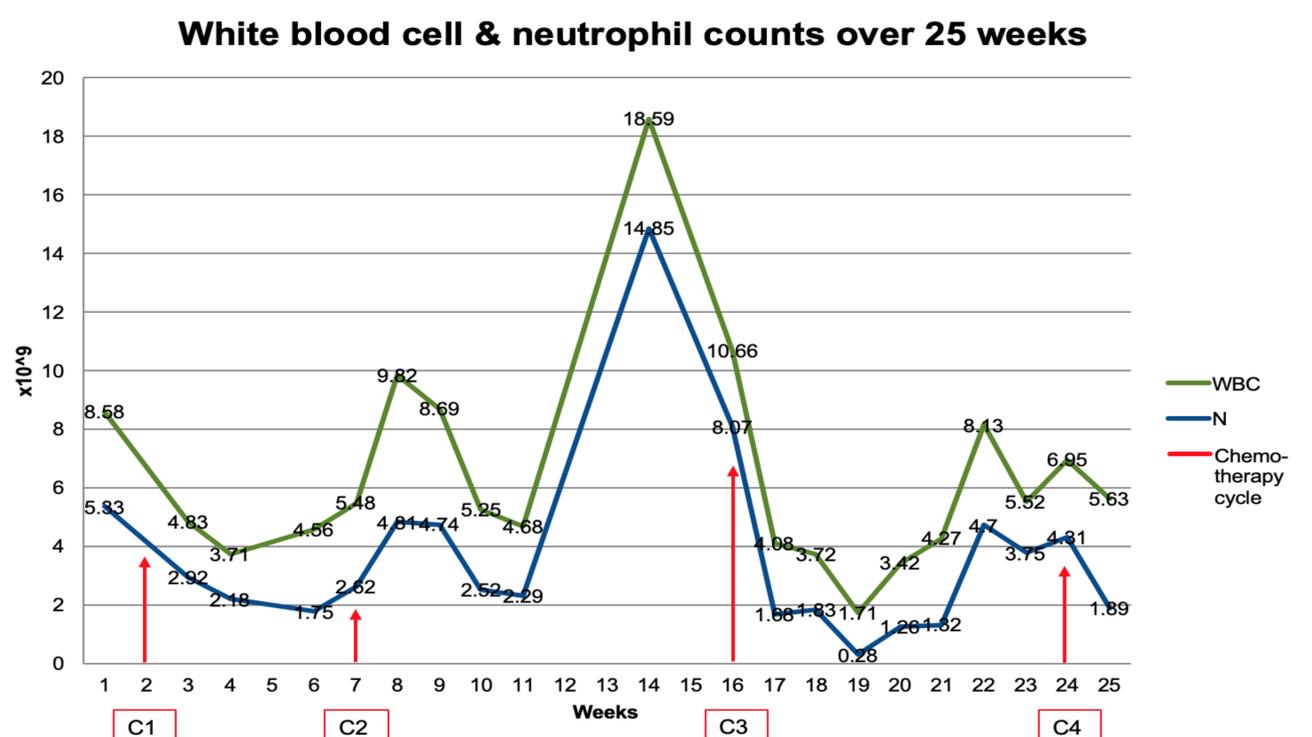
### Pharmacist's Role

- Monitoring full blood count (FBC)
- Liaison with ClopineCentral<sup>®</sup>
- Education of HiTH staff to monitor physically for signs of agranulocytosis

Figure 1: ClopineCentral<sup>®</sup> Protocol

| Clozapine Blood Results Monitoring System |                                       |                                       |  |
|---|---------------------------------------|---------------------------------------|--|
| Range                                     | White blood cell count                | Neutrophil count                      | Action   |
| Green                                     | Greater than 3.5 x 10 <sup>9</sup> /L | Greater than 2.0 x 10 <sup>9</sup> /L | Continue clozapine. <sup>4</sup>   |
| Amber                                     | 3.0 to 3.5 x 10 <sup>9</sup> /L       | 1.5 to 2.0 x 10 <sup>9</sup> /L       | Continue clozapine with twice weekly blood tests until return to green range. <sup>4</sup>   |
| Red                                       | Less than 3.0 x 10 <sup>9</sup> /L    | Less than 1.5 x 10 <sup>9</sup> /L    | Cease clozapine. <sup>4</sup> Daily blood tests until return to green range. <sup>4</sup> Monitor for signs of infection. <sup>4</sup> |

Graph 1: White blood cell and neutrophil counts over 25 weeks



### Management Plan

- Weekly FBC
- ClopineCentral<sup>®</sup> notified – accepted clozapine to be continued with chemotherapy
- Close monitoring of mental state for the first 2 weeks
- Cisplatin dose to be split over days 1 and 8 due to impaired renal function
- Omit (rather than delay) gemcitabine/cisplatin cycle if neutropenic and review prior to next cycle
- Administration of filgrastim 300microg on day 2 of each cycle

### Case Progress

DA was referred to NMHS – MH Hospital in The Home (HiTH) by his community mental health clinic for observation and closer monitoring of his mental state during the first 2 weeks of gemcitabine/cisplatin treatment.

As anticipated, the white blood cell (WBC) and neutrophil (N) counts trended downwards after each cycle of gemcitabine/cisplatin (see Graph 1 above for details). Administration of filgrastim successfully increased the neutrophil count to allow clozapine treatment to continue.

Outcome:

At the time of writing, Mr DA is about to undergo his 5<sup>th</sup> cycle of gemcitabine/cisplatin and his mental state remains stable.

### Discussion

The use of clozapine in combination with other agents that depress bone marrow function is not recommended.<sup>5</sup>

Ideally, clozapine should be withdrawn prior to chemotherapy, however this is not appropriate for many patients as a relapse of schizophrenia is undesirable and will most likely affect capacity to consent to chemotherapy.<sup>2</sup>

If clozapine is to be continued, it is essential to have a comprehensive management plan in place which is developed and agreed upon by all clinicians involved, the patient and the clozapine monitoring service.

### Considerations when developing a management plan:

1. Frequency of blood tests<sup>2</sup>
2. Actions to be taken if the WBC or N fall below the accepted minimum<sup>2</sup>
3. If and when clozapine should be stopped<sup>2</sup>
4. When to consider agents such as lithium and granulocyte-colony stimulating factor (G-CSF).<sup>2</sup>  
Lithium may be used in combination with clozapine to increase a patient's baseline WBC and N count, who would benefit from clozapine treatment; as well as speeding recovery of WBC count.<sup>2,6</sup> Filgrastim (a G-CSF) accelerates neutrophil recovery<sup>7</sup> and may be considered as a treatment option when neutropenia or leukopenia occur.<sup>2,6</sup>

### Conclusion

With more frequent and comprehensive monitoring and the use of filgrastim, clozapine treatment may be continued concomitantly with chemotherapy successfully.

### For further information please contact

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References available on request.  
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