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Title

Daratumumab effectiveness in heavily pretreated immune thrombocytopenia patients: a Case Series

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Introduction

Immune Thrombocytopenia is an acquired immune mediated peripheral destruction of platelets. It is a relatively common disease, with incidence 3.9 per 100,000 per year. Treatment is generally indicated when the platelet count is < 30 X 10^9 /L. First line treatment of immune thrombocytopenia is corticosteroids. Approximately 80% of adult patients with ITP have treatment failure with corticosteroids or become dependent on them and require second-line therapy. Second-line and subsequent therapies includes Rituximab, thrombopoietin receptor agonists, splenectomy, fostamatinib, and other immunosuppressive therapies. The response rate of second and subsequent therapies is variable, and some patients relapse after multiple treatment lines.

Daratumumab is an anti-CD-38 monoclonal antibody which targets plasma cells and primarily used for the treatment of multiple myeloma. Plasma cells are responsible for the production of antiplatelet antibodies. Multiple case series and case reports has showed that daratumumab is effective for the treatment of immune thrombocytopenia and autoimmune cytopenia. Here, we report our center experience with the use of daratumumab in the treatment of heavily pretreated immune thrombocytopenia patients.

Methodolgy

We conducted a review of all patients with the diagnosis of immune thrombocytopenia who received daratumumab in our center. Informed consent has been obtained from all patients. The study received institutional review board approval. The dose of daratumumab was 16 mg/kg and it is uniform across all patients. Number and frequency of doses varied and were based on physician's discretion as there are no standards. All patients received paracetamol, diphenhydramine and steroids (dexamethasone, hydrocortisone or methylprednisolone) as pre-medications. We followed the International Working Group(IWG) definitions for response assessment, where "complete response, CR" is defined as platelet count >100 X 10^9/L and no bleeding symptoms, "response, R" is defined as platelet count > 30 X 10^9/L or at least a twofold increase from the baseline count and no bleeding symptoms and "no response,NR" is defined as platelet count < 30 X 10^9/L, < a twofold increase from the baseline count, or presence of bleeding symptoms.

Results

Four patients received daratumumab for immune thrombocytopenia. The median patients age is 27(Range, 17-49) . The median number of previous therapies is 6 (Range, 5-8). One patient have had previous splenectomy (#3). At the time of starting daratumumab, the median disease duration was 6 years (Range, 4-12).

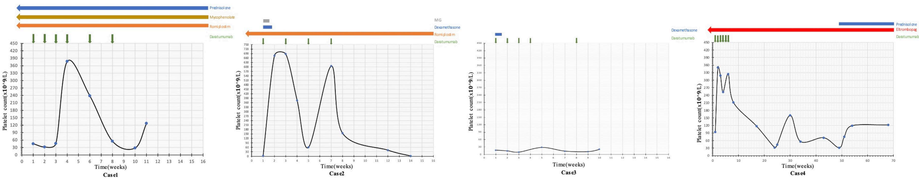
Three patients (#1, #2, #4) achieved complete response. Median time to response was 2 weeks (Range, 1-4 weeks). Duration of response was 10, 14 and 68 weeks, respectively. Patient #1 and #2 have relapsed while patient #4 has ongoing complete response. patient #3 had no response. Patient number #4 have had a drop in platelet count to 31 x10^9/L at week 49, for which she was started on tapering dose of steroids.

There was no major adverse events except for mild infusion reactions (patient #1, #2, #4) that has resolved with manipulation of infusion rate and supportive measures(steroids/antihistamines). There was no hematological toxicity and no infections.

Table 1: characteristics and outcome of patients.

Patient number	Age/Sex	Other underlying diseases	Previous splenectomy	Previous therapy	Number of Daratumumab infusions	Treatments given with daratumumab	Response	Duration of response (weeks)	Time to response (weeks)	Relapse
1	17/Male	None	No	Steroids(CR) Rituximab(NR) Eltrombopag(CR) Romiplostim(CR) Mycophenolate (NR)	6	Romiplostim Mycophenolate Prednisolone	CR	10	4	Yes
2	23/Female	Vitamin D deficiency Iron deficiency anemia	No	Steroids(CR) IVIG(CR) Rituximab(CR) Eltrombopag(NR) Romiplostim(CR) Azathioprine(NR)	4	Dexamethasone Pulse IVIG(for 2 days) Romiplostim	CR	14	1	Yes
3	31/Female	Iron deficiency anemia	Yes	Steroids(NR) IVIG(NR) Rituximab(NR) Splenectomy(NR) Eltrombopag(CR) Romiplostim(NR) Avatrombopag(NR) Azathioprine(NR)	5	Dexamethasone pulse	NR	NR	NR	NR
4	49/Female	Vitamin B12 deficiency Iron deficiency anemia Vitamin D deficiency	No	Steroids(CR) IVIG(CR) Rituximab(CR) Eltrombopag(CR) Romiplostim(CR) Azathioprine(NR)	6	Eltrombopag	CR	Ongoing	2	No

Figure 1: Evolution of platelet count in patients after Daratumumab.



Conclusion

Daratumumab shows clinical benefit for the treatment of immune thrombocytopenia in the heavily pretreated Immune thrombocytopenia patients. Our data demonstrate response rate of 75%. The onset of response was rapid (median of 2 weeks). Response was not durable in 2 out of the 3 patients who responded. One patient continues to be in remission after 68 weeks of follow up.

Recommendation

Larger studies are needed to confirm the benefit of of daratumumab in immune thrombocytopenia. Additionally, more research is needed on the optimal daratumumab dosing, frequency and the role of daratumumab maintenance in responders.

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