ELIGIBILITY:
- Biopsy proven symptomatic HIV negative, HHV-8 negative, multicentric Castleman’s disease

TESTS:
- Baseline (required before first treatment): CBC & diff, platelets, hemoglobin, creatinine, bilirubin, ALT, LDH, CRP
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with further treatment): HBsAg, HBcoreAb, hepatitis C antibody
- **Cycle 1 to 4**: Prior to treatment: CBC & diff, platelets
- **Cycle 5 and subsequent cycles**: Prior to alternate cycles i.e., even numbered cycles

PREMEDICATIONS:
(Note: patients should bring their own supply)
- diphenhydRAMINE 50 mg PO q 4 h during the IV infusion
- acetaminophen 650 to 975 mg PO q 4 h during the IV infusion

SUPPORTIVE MEDICATIONS:
If HBsAg or HBcoreAb positive, start lamIVUDine 100 mg/day PO for the duration of siltuximab therapy and for six months afterwards.

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>siltuximab</td>
<td>11 mg/kg</td>
<td>IV in 250 mL D5W over 1 hour</td>
</tr>
</tbody>
</table>
Administer using a 0.2 micron in-line filter |

Repeat every 3 weeks until disease progression. Reversal of all symptoms is achieved in most patients; shrinkage of lymphadenopathy is induced in a substantial minority. Continued control of the symptoms requires indefinite administration of the siltuximab although it is often possible to lengthen the intervals between doses. After greater than 6 months of continued control the interval between doses can be lengthened to the maximum that maintains complete symptomatic control.
DOSE MODIFICATIONS:

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>siltuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1 and greater than or equal to 50</td>
<td>less than 50</td>
<td>100% delay until recovery</td>
</tr>
<tr>
<td>less than 1 or less than 50</td>
<td>delay until recovery</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemoglobin* (g/L)</th>
<th>siltuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 170</td>
<td>100%</td>
</tr>
<tr>
<td>greater than or equal to 170</td>
<td>delay until recovery</td>
</tr>
</tbody>
</table>

*siltuximab may increase hemoglobin levels in MCD patients

PRECAUTIONS:

1. **Hypersensitivity:** Infusion related reactions most commonly involve pruritus, erythema, chest pain and nausea. Anaphylaxis may rarely occur (1.2%). Once resolved, siltuximab may be reinitiated at a lower infusion rate. See BC Cancer Hypersensitivity Guidelines.

2. **Infection:** Siltuximab may mask signs and symptoms of infection. Do not administer in patients with a severe infection, until the infection has resolved. Fever or other evidence of infection must be assessed promptly and treated aggressively.

3. **Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with lamiVUDine during chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA test at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

4. **Gastrointestinal Obstruction or Perforation:** There have been rare reports of gastrointestinal obstruction or perforation. Use with caution in patients at risk for perforation. Symptoms possibly indicative of such complications should be carefully investigated and appropriately treated.

Call Dr. Alina Gerrie or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References: