



Metastatic bladder cancer is cancer that has spread outside of the bladder, and it is treated with medication that goes everywhere in the body. A cancer initially grows by directly invading into that organ, but cancer cells can spread by travelling through the blood stream and the lymphatic vessels and eventually showing up as tumours or masses in other parts of the body. CT scans or MRIs are scans which determine the stage of the cancer. Bladder cancer tends to spread to lymph nodes first. If it's just a single lymph node in the pelvis (stage 3), we would often treat that with curative-intent options such as removal of the bladder or chemo with radiation. However, if it is spread beyond that, and scans show cancer in other organs, like the bones, the lungs, the liver, that is considered Stage 4 disease which is considered incurable. Stage 4 or advanced bladder cancer is aggressive but with newer treatments, patients can survive with good quality of life for years.

There has been a lot of research recently in this area and huge improvements have been seen with new combinations of treatments. In Canada, as of August 2024, the first treatment recommended is chemotherapy. A patient would be seen by a medical oncologist like myself, to determine eligibility for chemotherapy. This determination is based on how the patient feels, any other medical conditions they may have, how their organs are functioning, and the patient wishes. With all of this information, the medical oncologist can then recommend a chemotherapy regimen, usually cisplatin and gemcitabine, or carboplatin and gemcitabine. Patients are given four to six cycles of chemotherapy, which is medication delivered intravenously at the cancer centre. Each cycle is three weeks long and patients would have regular blood work and monitoring throughout treatment. CT scans are also done intermittently to check if the cancer looks smaller on those scans.

Chemotherapy kills rapidly dividing cells which can cause side effects as the chemo kills rapidly dividing cells. For example, mouth sores are common because the cells lining the mouth are rapidly dividing. Some people can get heartburn, nausea, vomiting, or bowel changes. Some patients can also develop neuropathy (numbness and tingling in their fingertips and toes) as well as kidney impairment due to the chemotherapy. Additional chemotherapy related side effects include a decrease in blood counts including red blood cells, white blood cells, and platelets. This means that the body may not be able to fight off infections as well while on chemotherapy. .

If a patient has had a good response to chemotherapy, which means that the cancer is either measuring smaller on CT scans, has disappeared, or is stable, then we prescribe maintenance immunotherapy with a medication called avelumab. This is immunotherapy which works differently from chemotherapy. With immunotherapy such as Avelumab, a much lower percentage of patients get side effects. Waking up the immune system is the goal of this therapy. We want the immune system to act against the cancer by recognizing it and sending inflammatory cells there to get rid of those cancer cells. The potential side effects can include things like diarrhea because the gut can be inflamed. It can include a skin rash, if it causes inflammation in the skin. It can include inflammation in our liver, which would show up on



bloodwork to show us elevated liver enzymes. Immunotherapy may impact any organ but usually this occurs in few patients.

We do have options that extend beyond chemotherapy if it doesn't work. In these situations, we would use a different immunotherapeutic agent called Pembrolizumab. If immunotherapy doesn't work or the cancer grows on immunotherapy, the next line of treatment is a medication called enfortumab vedotin. This is a newer medication called an antibody drug conjugate and it's a targeted drug delivery. We think about it as chemotherapy that's getting delivered into the cancer cell. So instead of getting a lot of side effects, there are fewer side effects due to this targeted drug delivery.

Some patients with bladder cancer or urothelial cancer harbor specific mutations in one of the genes in the cancer. We look for FGFR alterations, and if we find one, then that cancer may respond to treatment to a tablet form of treatment called Erdafitinib which targets these specific alterations.

Usually, these treatments are given in succession and patients are treated by the medical oncology team primarily.

As I mentioned, there has been a lot of research in this field in recent years and some very exciting data has led to a new treatment option. The combination of enfortumab vedotin and pembrolizumab immunotherapy was compared to chemotherapy as up-front treatment. The new combination led to improved responses and survival outcomes (patients lived longer with the new combination) on this large clinical trial. We are currently awaiting approval and funding for this combination, however I expect this to be the preferred option for most patients with metastatic bladder cancer when it becomes available.

To summarize, metastatic bladder cancer is an aggressive disease which is considered incurable. Treatment is aimed at increased survival and hopefully improving quality of life. There are now many options which novel combinations are anticipated soon.

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