For patients who have muscle invasive bladder cancer the standard treatment is to have the bladder removed or have bladder preservation (with chemotherapy and radiation). This is an aggressive cancer and despite aggressive treatment, up to 50% of patients will have the cancer come back. Cancer that has recurred would be outside the bladder and has often spread to other organs. This is called metastatic disease which is considered incurable.

In order to improve outcomes, we recognize that better treatments are needed. Patients with muscle invasive bladder cancer are treated by many specialists including a urologist, medical oncologist and radiation oncologist. Once the TURBT has been done and the diagnosis of muscle-invasion is confirmed, patients are referred to a medical oncologist to discuss neoadjuvant chemotherapy (chemotherapy delivered before surgery). The purpose of this treatment to try to kill any cancer cells which have escaped the bladder and are travelling in the body.

For bladder cancer, the cisplatin is the chemotherapy of choice in this setting. It is used in combination with another chemotherapy medication called gemcitabine. For patients who are very young and healthy, we might use a regimen which includes cisplatin is called dose dense MVAC (4 active chemotherapy drugs), which is slightly more effective but comes with a few more side effects.

Chemotherapy is given intravenously at the cancer center. Usually if we're giving cisplatin and gemcitabine, treatment is given on day one and day eight of a three week period. So a patient would have treatment two weeks in a row followed by a one week break. That three-week period is called one cycle. We would aim for four cycles or 12 weeks of treatment before surgery. Not everyone with muscle invasive bladder cancer is eligible for chemotherapy before surgery. One of the biggest reasons that patients are ineligible is because of their kidney function. If kidney function is impaired, we don't give cisplatin and would recommend the patient goes straight to surgery.

The patients' other medical conditions and general physical health are also important considerations when discussing this type of chemotherapy. Some patients are quite frail so this is not recommended. Also, patients who have baseline neuropathy (numbness and tingling in their fingertips and for example, from diabetes) would not be eligible for neoadjuvant chemotherapy as we know that cisplatin can make that worse. Similarly, if patients have underlying heart failure, or significant hearing loss, they may not be eligible for neoadjuvant chemotherapy. For suitable patients, we would proceed onto neoadjuvant treatment. Patients are monitored often by the oncology team during this time which is busy with blood work before each treatment, infusion appointments and scans. Usually halfway through treatment, the patient will get a CT scan done to make it looks clear and that there are no changes. It is important for patients to monitor and treat side effects immediately while on chemotherapy and to seek medical attention

with any major concerns. Once chemotherapy is complete (4 cycles or 12 weeks), the patient then recovers, and surgery is planned for approximately one month later.

The patients who were not eligible for neoadjuvant chemotherapy and who go for surgery first, sometimes come back to us after for a discussion about chemotherapy after surgery. If their kidney function is better, they may be a candidate for chemotherapy and we would consider that. The plan then would is the same chemotherapy – 4 cycles or 12 weeks of Cisplatin and Gemcitabine. The preference is for patients to get chemotherapy BEFORE surgery if they are well enough.

One relatively new treatment which is now available is immunotherapy after surgery for patients with high-risk disease. Studies showed that there are benefits to patients who either weren't eligible for neoadjuvant or adjuvant chemotherapy or patients who had actually received neoadjuvant chemotherapy and at the time of surgery still had a lot of cancer left over. For example, the pathology report still shows cancer that's invading into the muscle wall, or cancer that has gone into the lymph nodes. It’s in these patients where chemotherapy didn't do enough, or in patients who are not able to receive chemotherapy, where we now have the option of adjuvant nivolumab. This is also an intravenous treatment and is given once every two or four weeks for one year. The side effects in general with immunotherapy are less than with chemotherapy for most patients.

To summarize, it is important for patients with muscle-invasive bladder cancer to be considered for chemotherapy before or after surgery and immunotherapy. These treatments have been shown to improve the chances of survival. New treatments with new medications in combinations are currently being studied, so hopefully outcomes can improve further in this setting.

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