

## \*Perioperative Use of Avastin\*

This article responds to your request for information on the perioperative use of Avastin® (bevacizumab) in patients with cancer. This response was developed according to the principles of evidence-based medicine, with information from clinical trials, practice guidelines and systematic literature reviews.

### In brief

- Avastin may impair the wound healing process and can induce postoperative wound healing complications in patients.
- To avoid surgical wound healing complications, perioperative precautions are critical.
- Roche recommendations include
  - withhold Avastin for elective surgery
  - do not initiate Avastin for at least 28 days after surgery or until the surgical wound is fully healed, and
  - discontinue Avastin in patients who develop necrotising fasciitis.
- Published guidelines suggest stopping Avastin for 6-8 weeks before major surgery, and reinstate 4-8 weeks after major surgery. Furthermore, data exists regarding the use of Avastin in patients undergoing minor surgery.

### Precautions for the use of Avastin in the perioperative period

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Avastin may adversely impact the wound healing process due to its inhibition of angiogenesis. Wound healing complications are a known adverse drug reaction of Avastin and fatal events have been reported in clinical trials and in the post-marketing setting.<sup>1</sup>

Data from metastatic colorectal trials, showed that if patients were taking Avastin at the time of surgery, an increase in the incidence of wound healing complications arose within 60 days of surgery. The incidence of complications varied between 10% (4/40) and 20% (3/15).<sup>1</sup>

Therefore, to avoid surgical wound healing complications, perioperative precautions are critical. Refer to your local Avastin label for information on the use of Avastin before and after surgery.

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### Recommendations on the use of Avastin prior to major elective surgery

Various recommendations are available on the use of Avastin prior to major elective surgery. The interested reader is directed to the relevant references for further information.

#### Roche recommendation

Avastin should be withheld prior to major elective surgery. For your reference, the half life of Avastin is between 18-20 days.<sup>1</sup>

## **Guidelines from pivotal Avastin clinical trials**

In the pivotal Avastin clinical trials Avastin was withheld for between 4-6 weeks prior to a surgical procedure.<sup>2-14</sup>

Major surgical procedures were classed as invasive procedures requiring general anaesthesia, and included open biopsies.

### **Published guidelines and clinical opinion**

Published guidelines and clinical opinions are available which recommend to allow for at least 6 to 8 weeks between the last dose of Avastin and elective surgery;<sup>15-19</sup> this corresponds to two half-lives of Avastin.

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## **Recommendations on the use of Avastin after major elective surgery**

### **Roche recommendations**

Do not initiate Avastin for at least 28 days after major surgery or until the surgical wound is fully healed.<sup>1</sup>

Necrotising fasciitis including fatal cases, has rarely been reported in patients treated with Avastin<sup>1</sup>. Discontinue Avastin in patients who develop necrotising fasciitis.

### **Exclusion criteria in pivotal Avastin clinical trials**

Patients were excluded from the Avastin pivotal trials if they had major surgery within 28 days of study initiation.<sup>2-14</sup>

### **Published guidelines and clinical opinion**

Published clinical guidelines suggest that Avastin can be reinitiated once the surgical wound is healed.<sup>16-19</sup>

Additionally, the published guidelines provide a range of recommended delays before reinitiating Avastin treatment, from delays of at least 4 weeks<sup>15-19</sup> to delays of at least 6 to 8 weeks.<sup>20</sup>

Bose et al. proposed an individualised approach, whereby healthy patients with rapid wound healing could resume Avastin after 4 weeks, whilst patients with comorbidities impacting wound healing should extend the postoperative interval by re-initiating Avastin after 6 to 8-weeks.<sup>19</sup>

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## **Guidance on the use of Avastin in minor surgery**

Roche has no recommendations on stopping or starting Avastin in relation to minor surgery, such as the surgical implant of venous access devices. Timing of minor surgery would be a clinical decision, and local label must be consulted.

### **Pivotal Avastin clinical trials**

Minor surgery in clinical trials were classed as procedures not involving general anaesthesia or respiratory assistance.<sup>21,22</sup>

In clinical trials, minor surgical procedures, including fine needle aspiration, core biopsies, central venous access device placement, arose within 2-7 days of a patient's first dose of Avastin in the trial.<sup>9,22</sup>

Many of the Avastin clinical trial protocols do not provide guidance on when to resume Avastin after minor surgery, though one pivotal clinical trial's protocol mentioned that a treatment delay was not required for minor procedures such as removal or insertion of a central venous catheter.<sup>9</sup>

## **Published guidelines and clinical opinion on withholding Avastin following surgical implant of venous access devices**

There is limited evidence and lack of consensus regarding withholding Avastin treatment following surgical implant of venous access devices.<sup>15,23-26</sup>

Observational retrospective studies have demonstrated a reduced risk of subsequent wound complications associated with Avastin, if Avastin is withheld for a period of 7 to 14 days after device implantation.<sup>15,23-25</sup>

Other analyses provided an alternative view, stating that the complications in central venous port placement were not affected by the timing of Avastin initiation after port implantation.<sup>27,28</sup>

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