

EFFECTIVENESS AND TOXICITY OF HYPERTHERMIC ISOLATED LIMB PERFUSION WITH ANTITUMOR DRUGS IN TREATMENT OF IN-TRANSIT METASTASES OF MELANOMA AND SARCOMA

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Introduction and aims

Hyperthermic isolated limb perfusion (HILP) is a form of regional cytostatic treatment of locally advanced limb cancers. In HILP treatment the cytotoxic drugs (melphalan and/or TNF- α) are used under hyperthermic conditions. A particular problem presents the use of TNF- α , because this drug in pharmacological doses causes cardiogenic shock and therefore the systemic use is not allowed. The Institute of Oncology Ljubljana is one of the few institutions which has a special accreditation for using TNF- α during HILP, approved in May 2010 after successful completion of external verification. HILP is indicated in patients with regionally advanced melanoma and in patients with limb sarcomas where amputation would be the only radical treatment.

The aim of this retrospective study was to assess the results concerning the regional and systemic toxicity and other postoperative complications in 51 cases of HILP with cytotoxic drugs (melphalan alone or in combination with TNF- α) for in-transit metastases of melanoma or sarcoma. A review of effectiveness of treatment with overall response rate is included.

Materials and methods

From September 2010 to June 2015, 45 patients with in-transit metastases from melanoma and 6 with sarcoma have been treated with HILP (chart 1). During the procedure, the artery and vein for lower/upper limb is isolated and connected to the heart-lung machine. In the first part of the procedure, the isolated limb is warmed up to about 40°C and leakage measurements with isotope are performed. If there is no leakage, cytotoxic drug is applied in the dosage 10-20 times higher than the maximal dosages during systemic application. At the end of this procedure, the limb is washed out and the vessels repaired. The Wieberdink grading system was routinely used to evaluate the regional toxic effect of HILP. Most systemic side effects are caused by leakage of drugs into the systemic circulation during HILP.

Results and discussion

Regional toxicity after perfusion is classified using a 5-grade Wieberdink system (chart 3). In 70,58% (36) of patients no reaction occurred (I), 5,88% (3) of patients had slight erythema and/or edema (II), 3,92% (2) of patient had considerable erythema and/or edema with some blistering (III), 5,88% (3) of patients had extensive epidermolysis and/or obvious damage to the deep tissues, causing definite functional disturbances; threatening or manifest compartmental syndrome (IV) and 1,96% of patient had major reaction with amputation (V). In 6 cases of HILP systemic toxicity occurred; 3,92% (2) of patients had muscle wasting with elevated myoglobin, 1,96% of patient had thrombosis and 5,88% (3) of patient had systemic inflammatory response syndrome SIRS. 10 patients had treatment-related complications: 3 cases of swelling and pain in the treated limb, 3 cases of bleeding, 1 case of paresis and 3 cases of infection needed antibiotic treatment.

The overall response rate was 90,19%, including 83,67% complete and 6,52% partial responses of HILP. The progressive disease response duration was 3-10 months from the time of HILP.

CHART 1: Number of patients treated with HILP with melanoma or sarcoma in 5 years

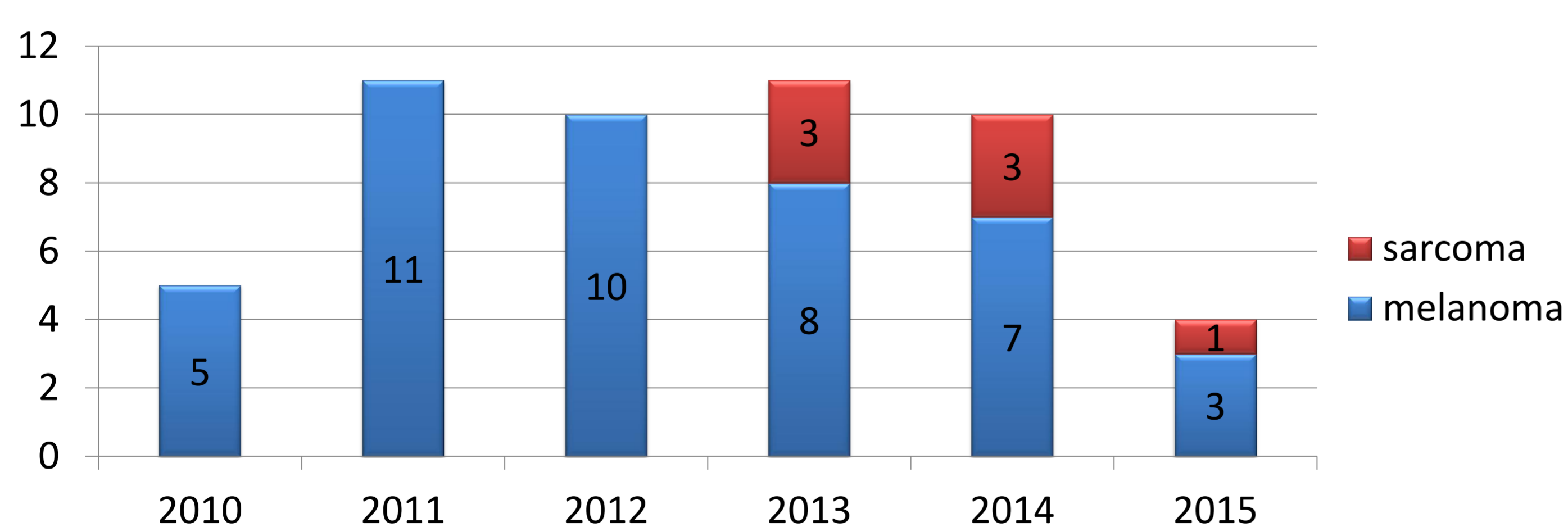
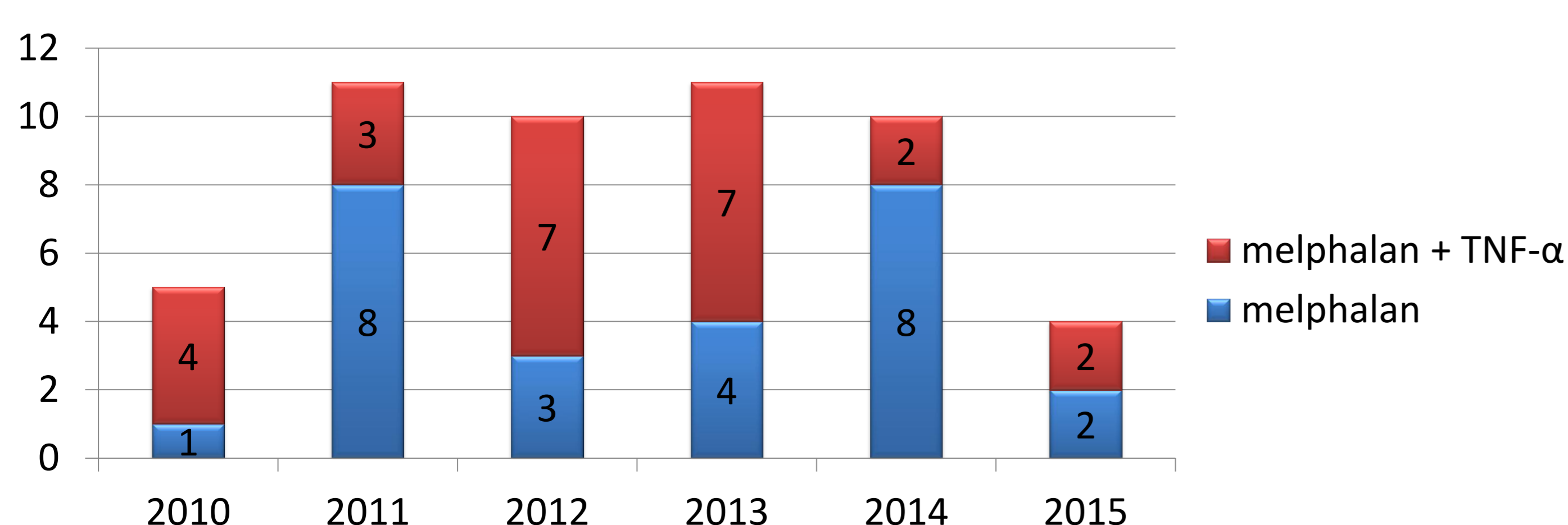


CHART 2: Drugs used in HILP (melphalan only or addition of TNF- α)



Results and discussion

CHART 3: Regional toxicity (Wieberdink classification)

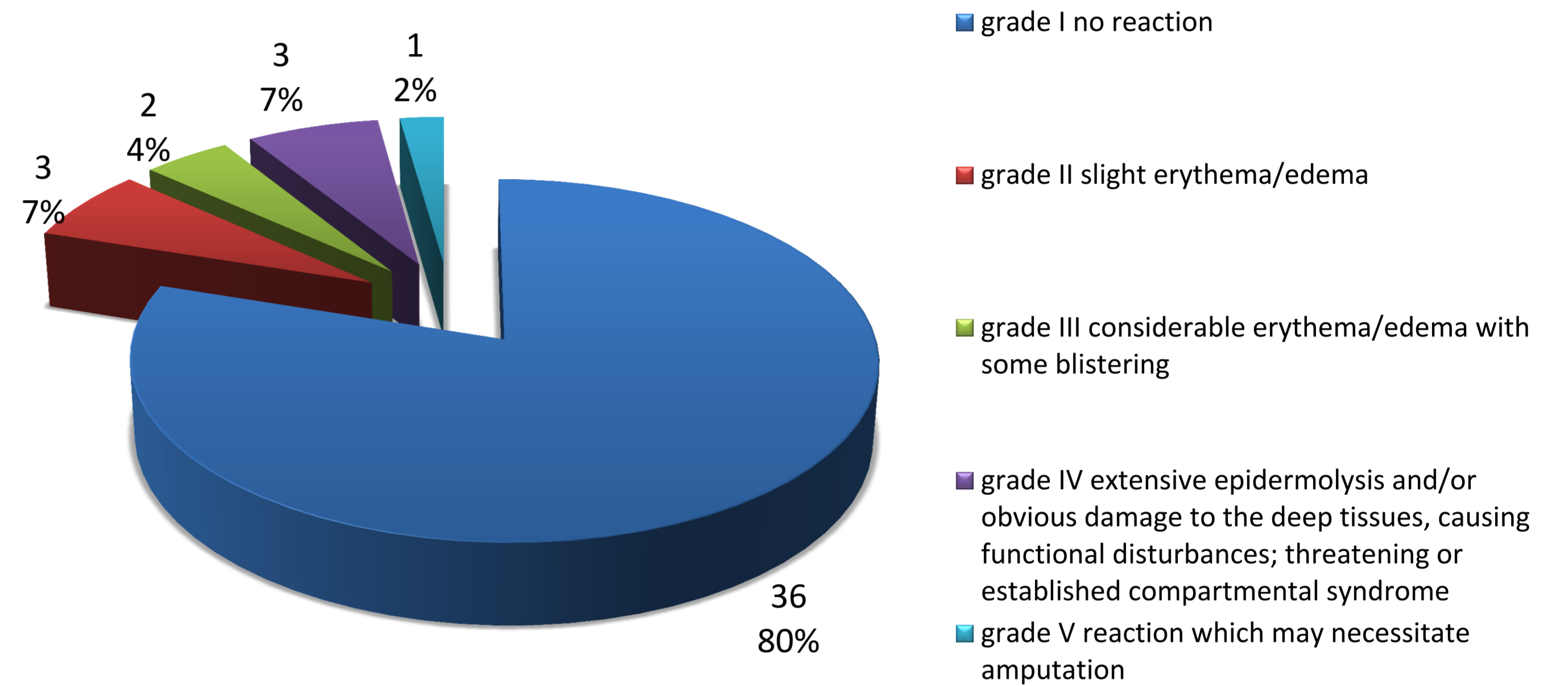


CHART 4: Systemic toxicity

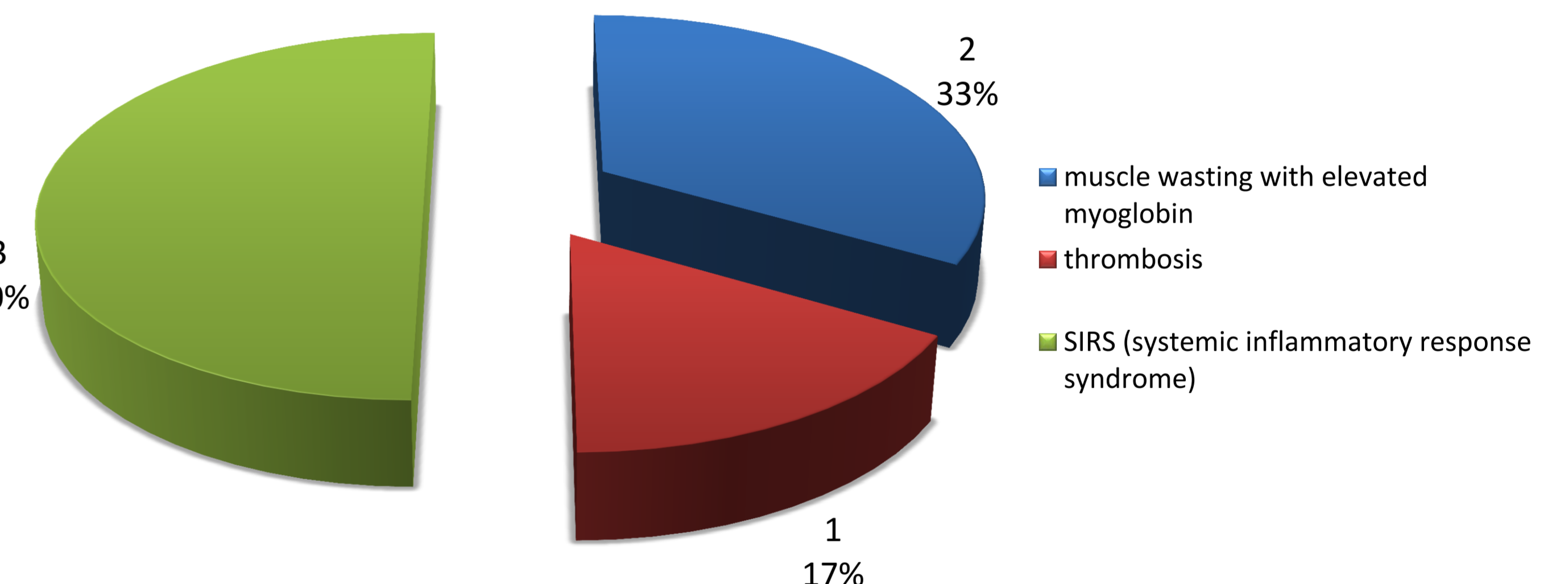


CHART 5: Treatment related complications

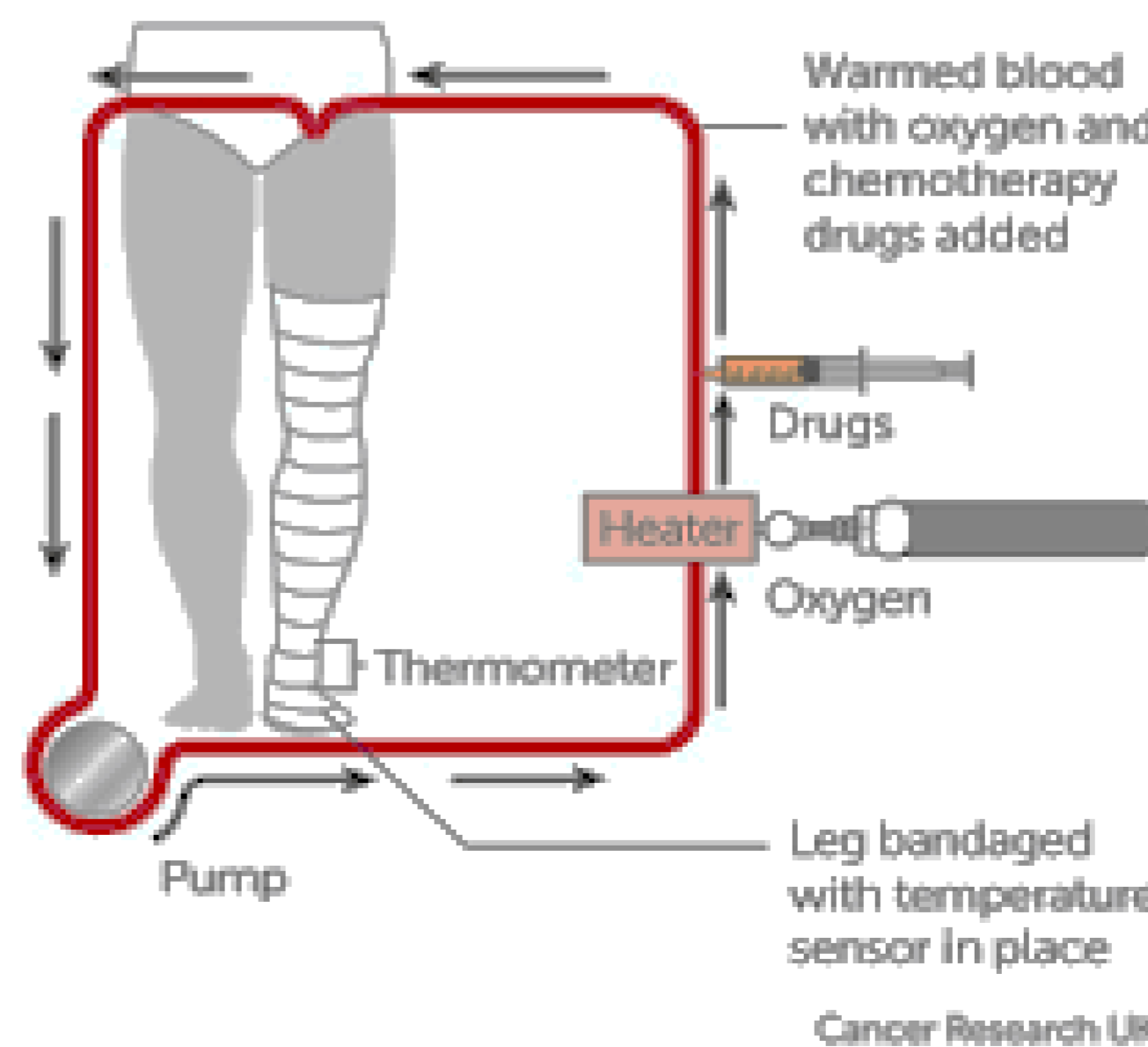
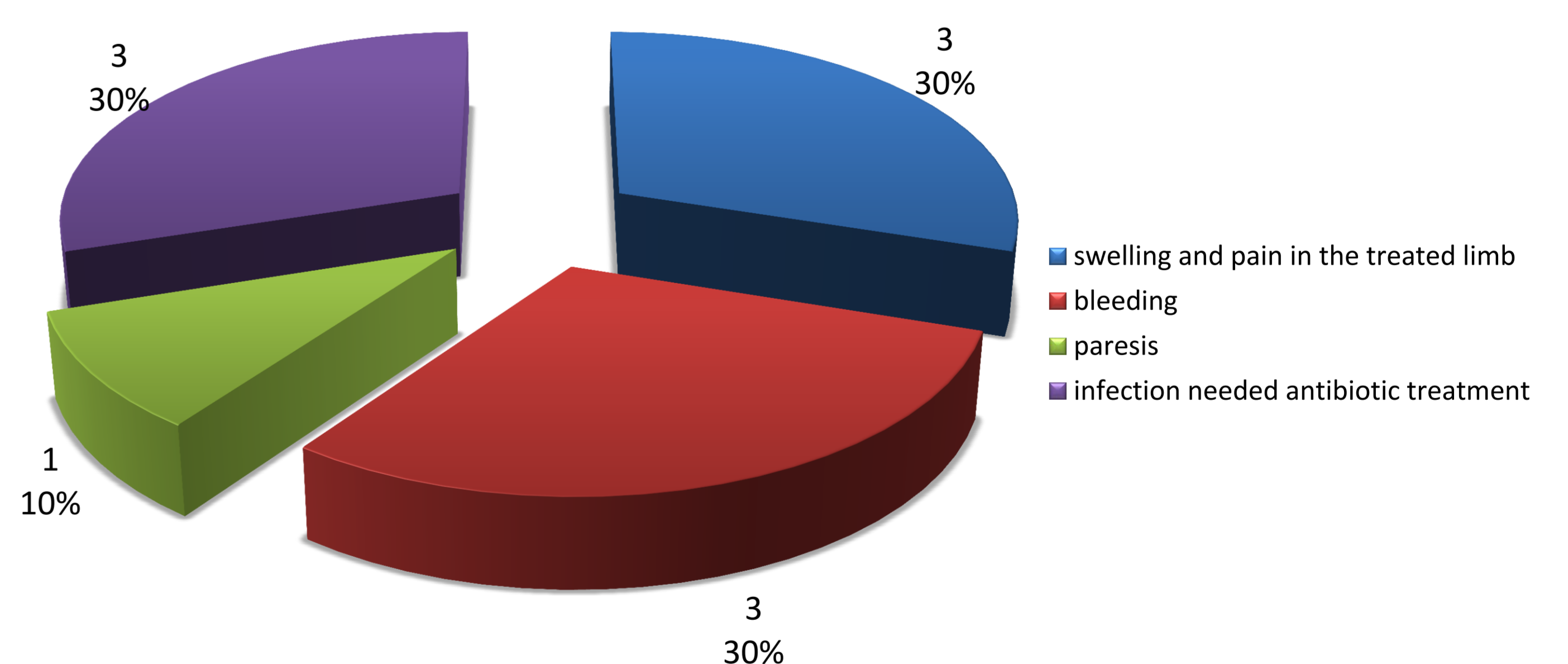


Figure 1: Schematic HILP



Figure 2: In-transit metastases

Conclusions

HILP is an effective treatment with complete response rates reaching up to 90% in patients with melanoma or sarcoma. Due to the systemic and local toxicity of cytotoxic drugs, close collaboration between clinical pharmacist and doctor during HILP is highly recommended.