The prognosis of advanced penile carcinomas is extremely poor. Low numbers of available studies on chemotherapy over a long time, decentralized treatment as well as rareness of disease have not improved the prognosis. This article focuses on important clinical trials and developments for chemotherapy in penile cancer. Considering the latest study data there is a strong recommendation for multimodal approaches, including lymph node dissection and perioperative treatments with cisplatin/taxane-based chemotherapy. A systematic, centralized registration and evaluation by the "Rostocker-AUO-Register" for penile cancer should improve conditions for affected patients. Furthermore, molecular targeted therapy might be a promising therapeutic option but until now only very few case reports have been published. Further prospective clinical trials are necessary to establish these agents in the therapeutic landscape of penile cancer. Decision for palliative chemotherapy in advanced penile cancer should be well considered and depends on the patient's age and general condition particularly regarding possible adverse events of chemotherapy. Notably, best supportive care might be an important alternative for some patients and should be taken in consideration.