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The use of antibiotic prophylaxis in patients with solid tumours — when and to whom?

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ABSTRACT

Cancer patients treated due to solid tumours are exposed to bacterial, fungal, and viral infections, and the high morbidity connected to them is caused by cancer itself and anticancer therapy. Systemic chemotherapy and local treatment, e.g. surgery and/or radiotherapy, can contribute to infectious complication, which have a negative impact on the efficacy of the treatment and patients' quality of life. Therefore, there is a need to look for prevention methods, and antibiotics might be one of the options. Since granulocyte colony stimulating factors (G-CSF) appeared, the use of antibiotic prophylaxis was limited to a few indications. In patients with afebrile neutropaenia the use of antimicrobial therapy should be considered only when coexisting risk factors exist. There are also certain situations in cancer therapy when antibiotic prophylaxis could be useful. The presented publication is aimed to identify situations when the treating clinician should consider antibiotic prophylaxis in a patient with a solid tumour.
Key words: antibiotic therapy, prophylaxis, chemotherapy, G-CSF, solid tumour

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Introduction

Cancer patients are exposed to infectious complications due to underlying malignancy, concomitant diseases, as well as anticancer treatment. Therapeutic modalities, supportive care, and prophylactic methods are determined by cancer type and also its location and stage at diagnosis. There are significant differences among treatment complications between elderly patients with internal concomitant diseases and lower performance status and young patients, who generally do well despite even more advanced cancer. Finally, some diagnostic and treatment procedures imply specific prophylactic methods, which aim to limit infectious diseases, improve quality of life, and optimise anticancer treatment. It should be also underlined that prophylactic antibiotic therapy should be employed when the expected benefits outweigh the possible risks of side effects like allergic reactions, *Clostridium difficile* infection, or resistant strains selection.

The following sections present the situations in which health care professionals should consider prophylactic antibiotic therapy as well as when this is not recommended.

General recommendations

The sensitivity of solid tumours to chemotherapy varies greatly. Cytotoxic drugs affect not only cancer cells but also normal human tissues. Fast growing cells, like mouth and gastrointestinal (GI) tract mucosa or haematopoietic cells, are especially susceptible. Time to mucosa or bone marrow toxicity usually ranges from 7 to 14 days, but it depends on the normal cell mitosis rate in these organs as well as on the type and dose of chemotherapy. Simultaneous damage of GI mucosa and/or bone marrow suppression contributes to infectious complications. The use of G-CSF is an acknowledged method of prevention of infectious complications of expected neutropaenia in patients after chemotherapy. Primary G-CSF prophylaxis beneficially influences the prevalence and duration of febrile neutropaenia, risk of bacterial infections, antibiotic therapy

duration, and number of days with hospitalisation. However, the impact of this method on decreased risk of death has not been confirmed yet [1]. The decision regarding introducing of G-CSF is mainly — but not entirely — based on the type of cancer and its chemotherapy. Primary prophylaxis of febrile neutropaenia with G-CSF is justified when chemotherapy with high risk index of febrile neutropaenia (> 20%) is used. In patients treated with chemotherapy of moderate risk of febrile neutropaenia (10–20%) the reasons for G-CSF introduction include the presence of additional risk factors and the occurrence of febrile neutropaenia complications (age > 65 years, higher stages of cancer, metastases to bone marrow, low performance status, previous radiotherapy on large area of bone marrow, malnutrition, female gender, anaemia, and kidney and liver impairment). Secondary prophylaxis with G-CSF should be considered in radically treated patients [2].

The use of antibiotics in primary prophylaxis of infectious complications is much more complicated. A meta-analysis of over 100 clinical trials, including 13,000 patients, published in 2012 showed significant benefits in terms of decreased mortality (of any causes) after prophylactic antibiotic therapy in patients during chemotherapy with neutropaenia but without febrile neutropaenia as compared to placebo or no prophylaxis. Additionally, it was noted that patients who underwent prophylaxis have decreased risk of death due to infection, risk of febrile occurrence, infection (clinically overt or microbiologically confirmed), and bacteraemia. The benefits outweighed potential risks of adverse events or inducing of drug-resistance. This treatment included: quinolones, trimethoprim-sulfamethoxazole (co-trimoxazole), systemic antibiotics (cephalosporins, vancomycin), and antibiotics unabsorbed from the GI tract (polymyxin, colistin, and neomycin). However, the majority of patients included to this meta-analysis were diagnosed with haematological malignancies [3]. A British study published in 2005, in which over 1500 patients received prophylaxis with either levofloxacin or placebo (nearly 90% of included patients had solid tumours), indicated decreased risk of febrile infection and hospitalisation in patients in the prophylactic group. The majority of patients received chemotherapy of low or moderate risk of febrile neutropenia. There were no differences between groups regarding mortality due to infection [4]. As patients with solid tumours treated with standard chemotherapy are usually put at low general risk of infection (neutropenia duration < 7 days), American recommendations do not qualify those patients for use of antibiotic in prophylaxis of bacterial infections [5]. However, use of additional antibacterial prevention is justified in selected patients with neutropaenia in order to decrease the prevalence of serious infectious complications, delay the occurrence of infection, as well as decrease a hospitalisation rate. The group at high risk of infectious complications includes patients with expected time of Grade 4 neutropaenia according to CTCAE (common terminology criteria for adverse events) exceeding 7–10 days. As a result, the final decision regarding introduction of prophylactic antibiotic therapy is influenced by the type of chemotherapy, type of cancer and its stage, as well as previous episodes of febrile neutropaenia. Additional factors indicating the need for prophylactic use of antibiotics include: older patient's age, concomitant diabetes, chronic lung disease, interrupted continuity of skin or mucosa, expected inflammation of mucosa after chemotherapy, and body overloading with iron [6]. Fluoroquinolones (ciprofloxacin and levofloxacin) are the most commonly used antibiotics in antibacterial prophylaxis. It was shown that the use of fluoroquinolones decreases the prevalence of febrile neutropaenia and infections microbiologically confirmed as compared to placebo or no prophylaxis [3, 4]. Additionally, these antibiotics less frequently induce resistant strains as compared to co-trimoxazole, fewer adverse events, and also adverse events leading to discontinuation of the treatment [3]. Fluoroquinolones could be used in antibacterial prophylaxis in patients with high risk of febrile neutropaenia after exclusion of local bacterial resistance to this group of antibiotics. Ciprofloxacin is administered in the dose 2 × 500 mg daily, and levofloxacin in the dose 1 × 500 mg daily. Levofloxacin shows lower efficacy against *Pseudomonas aeruginosa* as compared to ciprofloxacin but is more active against Gram-positive strains, e.g. *Streptococcus*. It is not recommended to add to prophylaxis with fluoroquinolones another antibiotic, more active against Gram-positive bacteria, because this does not decrease the risk of death due to infection but increases the risk of GI complications and infections elicited by resistant strains. There is no specific recommendation regarding duration of antibiotic prophylaxis, which is usually introduced on the first day of chemotherapy or the day after its cessation, and the therapy is continued until yielding the risk of neutropaenia or until start of treatment with broad-spectrum antibiotics in patients with fever [7].

Some chemotherapy protocols include distinct recommendations regarding prophylactic antibiotic therapy, different than general, which result from the design of pivotal study being a base of introducing this therapy to clinical practice. For example, it is not recommended to use G-CSF during induction chemotherapy TPF (docetaxel, cisplatin, fluorouracil), which is indicated in patients with head and neck cancer (with a risk of febrile neutropaenia of 5–15%); however, all patients receiving TPF protocol in the clinical study received ciprofloxacin between cycle days 5 and 15) [8, 9].

Indications to use antibiotics and growth factors should be considered separately. It has not been investi-

gated in prospective clinical trials so far, which method is more efficient as well as the value of their simultaneous use was also not established. A report was published in 2015 [10], retrospectively analysing the prevalence of febrile neutropaenia in 340 breast cancer patients undergoing adjuvant chemotherapy TC (docetaxel, cyclophosphamide) and additionally receiving different methods of primary prophylaxis, e.g. G-CSF, antibiotic, or no prophylaxis. Febrile neutropaenia was diagnosed in 1%, 11%, and 32% of patients, respectively. The risk of this complication during chemotherapy according TC protocol exceeds 30%, so this amplified the recommendations to use G-CSF prophylactically, despite the low rate of febrile neutropaenia in a previous phase III clinical study. Nevertheless, antibiotic could be used if the patient does not tolerate growth factors or denies their taking.

Prophylaxis of pulmonary pneumocystis

Pulmonary pneumocystis is an opportunistic infection caused by fungus *Pneumocystis jiroveci*. More than half of the population are carriers of this microorganism. Immunocompetent individuals have no signs and symptoms but they can be a source of infection for susceptible patients. In immunocompromised patients, infection could cause severe respiratory distress, quite often leading to death. Among patients treated for solid tumours the most exposed to this infection are the patients persistently treated with corticosteroids and patients with gliomas, who have undergone adjuvant radiochemotherapy with temozolomide. American societies [11] recommend consideration of prophylaxis with co-trimoxazole in patients at risk of this complication, e.g. in patients treated with steroids in a dose of at least 20 mg prednisone (or 3 mg dexamethasone) daily for four weeks or longer. The prevalence of pulmonary pneumocystis in patients with gliomas accounts for approximately 1%, with mortality exceeding 50% [12]. In the study of Stupp et al. [13] this rate was even higher and was 3% (prophylaxis with pentamidine became mandatory after pulmonary pneumocystis diagnosed in the first two patients among the 15 included in the trial).

Other opportunistic infections observed in this group of patients include fungal infections, as well as cytomegalovirus, herpes zoster virus, herpes simplex virus, and hepatitis B virus infections. Temozolomide induces delayed myelosuppression, with its nadir at 5–6 weeks of treatment. The risk of opportunistic infections increases when CD4+ cell count drops below 200/μl or total lymphocyte count is lower than 500/μl.

Dutch researchers analysed available literature regarding indications to prophylactic antibiotic therapy in patients treated due to gliomas [12]. Pulmonary pneumocystis prevention is recommended when corticosteroids are administered in a daily equivalent dose of at least 3 mg of dexamethasone during more than three weeks and should be continued for one month after cessation of steroid therapy providing normalised CD4+ cells or lymphocyte count. Additionally, this kind of prophylaxis should be considered in the following situations:

— in elderly patients (> 65 years old) with pulmonary disease — prophylaxis should be stopped only when normal CD4+ cells and lymphocyte counts recover;
— in patients during immunosuppressive treatment after organ or bone marrow transplantation, with rheumatic diseases, connective tissue disease, or inflammatory bowel disease;
— in HIV-positive patients with CD4+ cell count below 200/μl at start of treatment;
— in patients with pulmonary pneumocystis or common opportunistic infections in their medical history.

Concluding: prophylaxis of pulmonary pneumocystis should be initiated in patients with lymphocyte count below 500/μl (or CD4+ cell count below 200/μl). This preventive treatment should be continued until normalisation of haematological parameters. The drug of choice is oral co-trimoxazole in the dose of 480 mg once daily or 960 mg three times a week. In the case of co-trimoxazole intolerance, pentamidine inhalations should be used (300 mg once every four weeks), dapson 100 mg once daily orally, or atovaquone 1500 mg daily orally [12].

Prophylaxis of skin complications during anti-EGFR therapy

The innovative therapies are connected with the new sort of treatment-related adverse event, which have not been observed during standard chemotherapy. Epidermal growth factor receptor (EGFR) is one of the molecular targets for new drugs used in oncology. EGFR plays a significant role in the development of non-small cell lung cancer (NSCLC), squamous cell head and neck cancer, colon cancer, and breast cancer. EGFR receptor is a member of the human epidermal growth factor (HER) family, containing four membrane glycoprotein receptors. EGFR protein could be indicated in the majority of tissues, including blood, the immune system, as well as nervous, musculoskeletal, digestive, respiratory, endocrine, and reproductive systems. EGFR expresses in keratinocytes, eccrine sweat glands and sebaceous glands, hair sheath, and vascular endothelial cells. Active receptor transmits a signal to intracellular space, which leads to a biological reaction, resulting in regulation of many processes, including proliferation, differentiation, cell cycle, migration, and cell survival [14]. There are two types of EGFR inhibitors: low-molecular tyrosine

kinase inhibitors (TKIs), competitively blocking of phosphorylation receptors, and monoclonal antibodies (mAbs) binding to extracellular receptor domains. Anti-EGFR monoclonal antibodies, like panitumumab and cetuximab are used in patients with metastatic colon cancer meeting molecular criteria (wild — type *KRAS* and *NRAS* genes in tumour cells). Low-molecular EGFR TKIs (erlotinib, gefitinib, afatinib) are used in patients with NSCLC with predominant adenocarcinoma histology and meeting specific molecular criteria (activating *EGFR* gene mutations in tumour cells).

Targeted and conventional therapies differ not only in terms of efficacy measures, but they also show distinct adverse event profiles. The most common complications during chemotherapy include haematological and general effects, and targeted therapy is characterised mainly by skin and mucosal changes.

EGFR inhibitors imbalance the proliferation and differentiation of keratinocytes. It could cause direct immune reaction and produce an inflammatory reaction with T-cell infiltration of hair follicles. Finally, it could subsequently result in rupture of the hair system with the influence of neutrophils and damage of sweat glands [15, 16]. Papulopustular rash is observed in more than 90% of patients treated with anti-EGFR antibodies, definitely limiting their quality of life [17]. Usually it occurs between 8 and 10 days after introducing of therapy. There are five grades of skin toxicity (CTCAE) depending on the intensity of symptoms [18]:

— 1 grade: papulopustular rash involving < 10% of body surface area ± pruritus and paraesthesia;
— 2 grade: symptoms as mentioned above and additionally papules and pustules covering 10–30% of body surface area;
— 3 grade: symptoms as mentioned above and additionally papules and pustules covering > 30% of body surface area, local inflammation — oral antibiotics are indicated;
— 4 grade: papules and pustules covering some body surface area without assessing the percentage, when accompanied by expansive, life-threatening inflammation demanding intravenous antibiotic use;
— 5 grade: death.

As compared to mAbs, the reaction after TKIs is less intensive. Grade 3 or 4 papulopustular rash is less common and occurs in up to 9% of patients [19, 20]. Skin changes, usually located on the face and upper trunk, definitely limit the patient's quality of life, and sometimes require modification or even discontinuation of the treatment.

As it has been proven so far that occurrence of skin toxicity during anti-EGFR therapy positively correlates with anticancer response, proper treatment of this complication is one the most important parts of management [21].

The management of skin changes depends on their intensity [22, 23]. In patients with grade 1 and 2 skin toxicities care preparations are used — moisturising creams containing urea, soft cleaning preparations, emollients, local antibiotics (clindamycin, erythromycin gel), local glucocorticosteroids, and oral antihistamines. In higher grades oral antibiotics (from the tetracycline group or others in cases of supra-infection of *Staphylococcus aureus* — honey-coloured scabs) and oral corticosteroids are additionally used. Despite this some patients need dose reduction of anti-EGFR treatment, postponement of the next dose, or even treatment discontinuation. Because of skin toxicity limiting efficient anticancer treatment currently there is a tendency to earlier introducing of skin changes therapy, e.g. oral antibiotics are more often used after the occurrence of first papulopustular lesions.

There are some observations supporting use of primary antibiotic prophylaxis in patients receiving anti-EGFR treatment. The phase II study STEPP in patients treated with panitumumab assessed the effect of primary prophylaxis with doxycycline 2 × 100 mg for six weeks on skin toxicity and quality of life compared to reactive treatment (doxycycline administration only after occurrence of skin changes). It was shown that skin toxicity of grade 2 or higher was 50% less frequent in patients receiving prophylaxis, and quality of life was also better in this group as compared to reactively treated patients [24].

In 2013 an Italian study was published in which lung cancer patients treated with erlotinib and colon cancer patients treated with cetuximab or panitumumab received prophylactically lymecycline in the dose of 300 mg daily. During the first three months of therapy grade 2 adverse reactions in the skin occurred in 27% of patients. A decreasing prevalence of serious skin toxicities with higher percentage of grade 1 changes was also indicated, without need for anti-EGFR dose reduction. Patients' quality of life was unchanged during the whole study [25].

Another Japanese study retrospectively analyzed 55 panitumumab-treated colon cancer patients. One group of patients received minocycline as a prophylaxis of skin changes and the rest was treated with minocycline only after occurrence of complications. Significantly less frequent complications were observed in group receiving primary prophylaxis, without any impact on efficacy of anti-EGFR therapy [26].

Use of tetracycline (2 × 250 mg for four weeks) in primary prophylaxis of skin toxicity was investigated in NSCLC patients treated with afatinib [27]. In total 90 patients were assigned to the group receiving tetracycline prophylactically and treated with antibiotic after occurrence of grade 3 or 4 toxicity. The frequency and intensity of skin complications during afatinib treat-

ment decreased by more than 60% and tetracycline was well tolerated.

The question arose, if acneiform rash is predictive factor of response to anti-EGFR treatment, could the use of tetracycline decreas treatment efficacy? Canadian researchers tried to address such a question [28] and retrospectively analysed 119 patients with advanced colon cancer treated with panitumumab or cetuximab. One group of patients received oral antibiotics in prophylaxis and the other after occurrence of rash. There was no difference between groups according to treatment efficacy, e.g. in both groups overall survival time and the number of anti-EGFR treatment cycles were similar.

Therefore, primary antibiotic prophylaxis in patients receiving anti-EGFR therapy decreases the frequency of higher grade skin toxicities and improves quality of life as compared to patients treated with antibiotics only after the occurrence of toxic signs. The MASCC Skin Toxicity Study Group recommends use of tetracyclines in prophylaxis, e.g. doxycycline in the dose of 100 mg twice daily for the first six weeks, and minocycline 100 mg daily for eight weeks. Doxycycline has a better safety profile, especially in patients with impaired kidney functions, whilst minocycline is less photosensitising (recommendation level IIa) [29].

Prophylaxis of urinary tract infections

Urinary tract infection is a common problem in patients treated due to solid tumours; however, there are no data regarding specific prophylaxis in this group of patients. Additionally, management of asymptomatic bacteriuria in these patients is also a very interesting topic. Prophylaxis is not recommended in otherwise healthy individuals (except pregnant women). Antibiotic prophylaxis is also not recommended for prevention of urinary tract infections in patients with non-infiltrating bladder cancer with asymptomatic bacteriuria and requirement of BCG therapy [30, 31]. The following section presents Polish recommendations regarding prophylaxis of urinary tract infection in the general population. It seems that patients treated due to solid tumours need individualised decisions regarding prophylaxis of urinary tract infection.

In patients with chronic urethral catheterisation routine antibiotic prophylaxis of urinary tract infection is not recommended. Female patients with recurrent non-complicated urinary tract infections in medical history (at least three episodes during year or at least two episodes during six months) benefit from antibiotic prophylaxis in terms of decreasing the number of urinary tract infection episodes, but with more frequent adverse events (vaginal and oral fungal infections, rash, nausea). Antibiotic treatment usually lasts 6–12 months. Administered drugs included: co-trimoxazole (240 mg daily or three times a week), trimethoprim 100 mg daily, ciprofloxacin 125 mg daily, cephalexin 250 mg daily, cefaclor 250 mg daily, nitrofurantoin 50–100 mg daily, norfloxacin 50–100 mg daily, fosfomycin 3 g every 10 days. However, the number of infections before and after initiating prophylaxis is often similar [32].

Numerous studies and meta-analyses did not confirm the efficacy of cranberry extract [33, 34].

Perioperative prophylaxis

Antibiotic prophylaxis is recommended during selected surgical operations, when the risk of surgical site contamination is high, e.g. operations in clean-contaminated surgical site (controlled opening of urinary, respiratory, or gastrointestinal tract without clear contamination with its content) or contaminated/soiled surgical site (operations with infringement of aseptic rules, chronic wound treated by transplantation, preoperative perforation of GI, biliary or respiratory tract) [35]. Prophylaxis is also recommended in all patients undergoing surgical operation, when the infection risk could be connected with serious disease or increasing mortality, e.g. during profound neutropaenia. The appropriate choice of antibiotic depends on the infection risk and possible aetiology of surgical site infection. It is said that antibiotic should be administered no earlier than two hours before operation (the most optimal timing is as short before operation as possible), and the subsequent doses are given depending on duration of procedure and lost blood volume. Total duration of prophylactic antibiotic treatment is limited to 24 or 48 hours (in the majority of cases the antibiotic is administered once) [36].

In thoracosurgical oncology operations (lung resection, lobectomy, thoracotomy) antibiotic prophylaxis is routinely used in all patients (cefazolin, cefuroxime, amoxicillin/clavulanic acid, and ampicillin/sulbactam). Typical infections include surgical site infections, tracheobronchitis, pneumonia (more frequent in pathogen carriers with concomitant chronic obstructive pulmonary disease), and lung abscess. The highest risk of postoperative pneumonia is during the first days after operation and during hospitalisation in the intensive care unit.

Patients undergoing oncology surgery of the GI tract are exposed to streptococcal infections as well as those caused by mouth anaerobes and Gram-negative bacilli, mainly *E. coli* in patients after operations of the upper GI tract and small intestine. In such cases antibiotics used in prophylaxis include cefazolin or alternatively amoxicillin/clavulanic acid, and in patients sensitive to beta-lactams — clindamycin or vancomycin in combination with aminoglycosides or fluoroquinolone. Potential

aetiological factors of infections in patients after large intestine operations include Gram-negative *Enterobacteriaceae* and anaerobes *Bacteroides* and *Clostridium*. The antibiotics used in these cases include cefazolin with metronidazole, ampicillin/sulbactam, ertapenem, and in patients allergic to beta-lactams — clindamycin (or metronidazole in combination with aminoglycosides or fluoroquinolone). During operations on the biliary tract (*Enterobacteriaceae*, enterococci, anaerobes) ampicillin/sulbactam or ceftriaxone are recommended, and in patients allergic to beta-lactams antibiotics as presented above. During gynaecological operations with abdominal or vaginal hysterectomy it is recommended to administer cefazolin (± metronidazole), ampicillin/sulbactam, or amoxicillin/clavulanic acid.

The risk of bacteraemia in patients undergoing urological operations with mucosal bleeding and with preoperative bacteriuria is significant, so the European Association of Urology (EAU) clearly recommends urine culture, the result of which implicates the choice of perioperative prophylaxis and its duration. The American Urological Association (AUA) recommends treatment of bacteriuria or decreasing of bacterial titre before operation and prolongation of treatment with antibiotics up to 24 hours after surgery [32]. In patients undergoing transrectal prostate biopsy or transurethral resection of the prostate (TURP) fluoroquinolone or co-trimoxazole are given, alternatively aminoglycoside (± clindamycin) [37, 38].

In patients undergoing head and neck cancer surgery perioperative administration of antibiotic in prophylaxis of infectious complications should be considered — clindamycin in combination with gentamycin single dose or amoxicillin/clavulanic acid or cefuroxime in combination with metronidazole [36, 39, 40].

Antibiotic prophylaxis is also recommended in patients undergoing oncology surgery due to breast cancer (single dose of cefazolin) [41].

Prophylaxis of skin and subcutaneous tissue infections

Routine prophylaxis with antibiotics is not recommended in patients with chronic skin changes like ulcerations, bedsores, and diabetic foot [42]. Antibiotic treatment in this group of patients is indicated in cases of general symptoms, broadening of infection to healthy tissues, like bones, muscles or fasciae, and should cover mainly Gram-positive cocci. The specific group of patients covers the patients with neutropaenia and chronic skin changes — in this case the antibiotic prophylaxis should be considered together with an assessment of additional risk factors of infectious complications (this was presented in previous parts).

Prophylaxis of infections in patients with ascites/hepatic encephalopathy

Patients with malignant ascites or those caused by secondary liver failure are usually during end-stage cancer. In these cases the management is either supportive or to improve quality of life. The use of antibiotics in prophylaxis should be limited to selected patients. In patients with ascites secondary to liver failure with concomitant bleeding prophylactic treatment with antibiotics (ceftriaxone 1 × 1 g daily for seven days, alternatively norfloxacin 2 × 400 mg) decreases the risk of bacterial complications as well as the mortality rate [43]. In patients with ascites caused by liver cirrhosis with low total protein concentration in peritoneal fluid (below 15 g/l) administration of norfloxacin (1 × 400 mg daily) could be considered because it reduces the risk of spontaneous peritonitis [44, 45].

Therapeutic and prophylactic management in patients with hepatic encephalopathy aims to decrease ammonia serum concentration indirectly by decontamination of the GI tract. In order to achieve this, lactulose (120–240 ml daily in 3–4 doses) or rifaximin (400 mg 3 times daily), unabsorbed from GI tract antibiotics from the rifamycine group, are administered. Both drugs are effective, but rifaximin gives fewer adverse events although it is the more expensive option [46–48].

Summary

The use of antibiotics in antibacterial prophylaxis in patients with solid tumours is justified only in specific situations. Fluoroquinolone prophylaxis should be considered in patients with the risk of long-term grade IV neutropaenia, in patients with additional risk factors, and in patients treated with specific chemotherapy protocols. Co-trimoxazole is effective in prophylaxis of pulmonary pneumocystis in patients with gliomas undergoing radiochemotherapy with temozolomide and in patients chronically treated with corticosteroids, and using of co-trimoxazole is recommended especially in cases of concomitant lymphocytopaenia. Antibiotics from the tetracycline group are used in prophylaxis of skin complications in patients receiving anti-EGFR treatment, because they decrease the frequency of those complications and improve quality of life as compared to use of these antibiotics only after the occurrence of clinically overt skin changes.

Perioperative prophylaxis in patients undergoing oncological surgery is also recommended. Prophylactic management in patients with higher risk of urinary tract infections, chronic skin lesions, ascites, or hepatic encephalopathy should be individualised based on their current clinical situation, without any universal recommendations.

However, the side effects of prophylactic antibiotic treatment should not be underestimated, and their risk should not outweigh the potential benefits.

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