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Tigecycline in the empiric therapy of fever in high-risk granulocytopenic haematologic cancer patients

Submission date	Recruitment status	[_] Prospectively registered
18/06/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
17/07/2012	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
06/10/2016	Cancer	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Cancer patients undergoing intensive chemotherapy can become granulocytopenic (low level of white blood cells), leaving them at high risk of developing infections, which may be lethal if antibiotic treatment is not promptly started. Currently, treatment with a single antibiotic is the standard treatment, but this approach may be inadequate due to the increasing number of infections caused by multi-drug resistant bacteria. To investigate the possible benefits of more aggressive antibiotic treatment, the aim of this study is compare the effectiveness of the antibiotic combination piperacillin-tazobactam with or without Tigecyclin, a new broad-spectrum antibiotic.

Who can participate?
Cancer patients, aged over 18, with fever and chemotherapy-induced neutropenia (low level of white blood cells)

What does the study involve?
Participants are randomly allocated to receive either piperacillin-tazobactam or piperacillin-tazobactam plus tigecycline. At the end of the study the success rates of the two treatments are compared. The response is considered a success if fever and clinical signs of infection are resolved and if the infecting microorganisms are eradicated without changing the allocated treatment. Patient survival is also assessed after 30 days.

What are the possible benefits and risks of participating?
The study's results may help to find the best way to treat bacterial infections in high-risk cancer patients. The main risk is the possible increased side effects with the combined antibiotic treatment. Therefore, participants are strictly monitored for the occurrence of side effects.

Where is the study run from?
28 cancer centres in Italy

When is the study starting and how long is it expected to run for?
May 2008 to November 2010

Who is funding the study?
University of Perugia (Italy)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2006-006210-14

Study information

Scientific Title
Prospective, randomised, multicentre controlled trial on empiric antibiotic therapy in febrile neutropenic cancer patients: piperacillin and tazobactam plus tigecycline versus piperacillin or tazobactam monotherapy

Study objectives
A more aggressive antibacterial approach with a combination regimen including Tigecycline, a new broad spectrum antibiotic, may be more effective than monotherapy.

Empiric antibiotic monotherapy is considered the standard of treatment for febrile neutropenic cancer patients, but this approach may be inadequate due to the increasing prevalence of infections caused by multidrug resistant bacteria.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Hospitals of Umbria Ethics Committee (Comitato Etico delle Aziende Sanitarie della Regione Umbria), 14/12/2006, ref: 13846/07/ACC

Study design
Prospective multicentre randomized controlled unblinded clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Febrile neutropenia/bacterial infections in immunocompromised cancer patients

Interventions
Patients were randomized to receive intravenous piperacillin-tazobactam or intravenous piperacillin-tazobactam plus tigecycline.187 were assigned to receive intravenous piperacillin-tazobactam and 203 to receive intravenous piperacillin-tazobactam plus tigecycline.

Over a period of two years, at each participating centers, febrile neutropenic cancer patients were assigned to receive an antibiotic monotherapy (piperacillin-tazobactam, 4.5 g intravenously every 8 hours) or a combination regimen (piperacillin-tazobactam, 4.5 g intravenously every 8 hours, plus tigecycline, 50 mg intravenously every 12 hours). The maximum duration of the treatment was 14 days.

At the end of the study we compared the success- rates of the two groups of treatment. We considered the response a success if fever and clinical signs of infection resolved and if the infecting microorganisms were eradicated without change of the initial allocated therapy.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Piperacillin, tazobactam, tigecycline

Primary outcome(s)
The success rates of the antibiotic regimens. We considered the response a success if fever and clinical signs of infection resolved and if the infecting microorganisms were eradicated without change of the initial allocated treatment. Response was defined as a failure if the patient died as a result of primary infection; if bacteremia persisted beyond the first 24 hours of therapy; if a breakthrough bacteremia was documented; if the isolated pathogen was resistant to the assigned antibiotics; if no response was seen after at least 72 hours of empiric therapy; if shock or acute respiratory distress syndrome or a disseminated intravascular coagulation or multiple organ failure was observed; if infection relapsed within 7 days of discontinuation of treatment;

and if toxicity occurred that required interruption of treatment.
Response was also evaluated by assessing survival at day 30.

Key secondary outcome(s))
Safety and tolerability of the two antibiotic regimens

Completion date
04/11/2010

Eligibility

Key inclusion criteria
1. Consecutive adult (>18 age)
2. Cancer patients were eligible for randomization if they had fever ((≥38.5°C on one occasion or ≥38°C on two or more occasions within 12 hours)
3. Chemotherapy-induced neutropenia (absolute neutrophils count less than 1000 per cubic millimeter anticipated to decrease to fewer than 500 cells per cubic millimeter within 24 to 48 hours) and a presumed infection
4. Patients were enrolled only once in the study and were hospitalized at the participating centres

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Had received any intravenous antibiotics during the preceding 96 hours
2. Had a known allergy to any of the protocol antibiotics
3. Had renal failure requiring hemo- or peritoneal dialysis or a serum creatinine level greater than 25 ml/min
4. Were pregnant or had known human immunodeficiency virus infection

Date of first enrolment
03/05/2008

Date of final enrolment
04/11/2010

Locations

Countries of recruitment
Italy

Study participating centre
Istituto di Medicina Interna e Scienze Oncologiche
Perugia
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Sponsor information

Organisation
University of Perugia (Italy)

ROR
https://ror.org/00x27da85

Funder(s)

Funder type
University/education

Funder Name
University of Perugia (Italy)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration