Targeted therapies

How you can manage the most common side effects

WALCE
Women Against Lung Cancer in Europe

Targeted therapies

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Taking into account your diagnosis, the nature of the disease and your overall health status, your doctor has prescribed a targeted therapy treatment.

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1. Introduction
What targeted therapies are

Each type of targeted therapy is associated with a specific mechanism of action, but all interfere with the ability of the cancer cells to grow, multiply, repair and/or communicate with other cells, with few effects on normal cells and consequently fewer side effects for the patients.

Targeted therapies act against a specific molecular target, such as a **protein**, a receptor, an **enzyme**, or the formation of new **blood vessels** (**neo-angiogenesis**) requested for the growth of the tumour.

Some of targeted therapies have more than one molecular target. Since clinicians and researchers call these molecules “molecular targets”, the therapies are also called “molecular targeted drugs”, “molecularly targeted therapies”. Targeted therapies will provide physicians a better way to tailor cancer treatment.
The research is moving toward individualized therapy, based on the unique set of molecular targets and/or genetic make up displayed by the cancer cells.

No indication may replace your oncologist, but it can be a useful support to cope with the treatment.

Targeted therapies interfere with cancer cell growth and reproduction in different ways.

The drug is distributed throughout the body and, despite its fairly selective mechanism of action, it can also interfere with normal cells and this is the cause of possible side effects.

Don't be afraid of side effects starting your treatment, because sometimes if you get more information about you can face them properly.

REMEMBER

- Every person does not get every side effect and some people get few, if any
- The severity of side effects varies greatly from one person to another and it is important to discuss with your doctor and nurse about them
- Your doctor may prescribe medication (named premedication) to prevent some side effects before they appear
- Although side effects can be unpleasant, they must be measured in the context of the treatment's ability to destroy cancer

How long do side effects last?

Most side effects gradually disappear after treatment ends, because the healthy cells recover quickly.

The time it takes to get over some side effects and regain energy varies from person to person and depends on many factors, including the type of therapy you are receiving and your overall health.

Patients often become discouraged about the length of treatments and side effects. This can make difficult the continuation of treatments: if you have this feeling talk to your doctor, who evaluates whether to adopt measures to counter them and whether to change your medication or treatment schedule (in terms of dose, type of drug, administration of it).

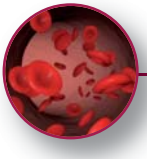
2. Haematological toxicity

Bone marrow produces three major blood components:

- Red blood cells, which carry oxygen to cells throughout the body
- White blood cells, which fight infections
- Platelets, which help blood clot and stop bleeding

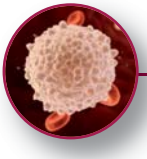
The targeted therapies (not in a such way as chemotherapy) can destroy some of the bone marrow cells so fewer blood cells are produced.

Haematological toxicity often requires the discontinuation of therapy and/or a dose reduction. It is up to your doctor to assess the scale and decide appropriate measures.



We talk about:

- ANEMIA: reduction of red blood cells circulation and therefore the haemoglobin, the protein contained in them which carries oxygen to tissues



- TROMBOCYTOPENIA (or PIASTRINOPENIA): reduction of the platelets circulating in the blood
- LEUCOPENIA: reduction of white blood cells number. NEUTROPENIA is the reduction of neutrophil number, which are one type of white blood cells, especially important in fighting infections

Which are the effects of haematological toxicity

In many cases haematological toxicity is asymptomatic (it does not cause any sign or symptom) and is highlighted only by blood tests periodically carried out.

ANEMIA
You may have these symptoms:

- **fatigue**
- **shortness of breath (named dyspnea)**
- **paleness**
- **tendency to feel cold**
- **dizziness**

LEUCOPENIA (and **NEUTROPENIA**) decreases your body's ability to fight infections. The reaction to this event depends on the extent of values decreasing (white blood cells and/or neutrophils number reduction) and on your overall health.

Infections can begin in almost any part of your body (mouth, skin, lung, intestinal or urinary tract, genital apparatus, etc.) and can be associated with fever.

Be alert to the signs and symptoms of infection and report to your doctor immediately:

- **Fever of 100.5° F (38.5° C) or greater**
- **chills**
- **sweating**
- **diarrhoea (it can also be a side effect of the therapy)**
- **burning feeling when you urinate**
- **cough (not present before or with different characteristics)**
- **redness and pain around the insertion of central access device**
- **abdominal pain**

PIASTRINOPENIA (or **TROMBOCYTOPENIA**): if your blood does not have enough platelets, you may bleed or bruise more easily than usual, even from minor injury.

Report these signs and symptoms to your doctor:

- **unexpected bruising (spontaneous and/or due to minor injuries)**
- **small red spots under your skin**
- **presence of blood in the urine and/or faeces or pinkish urine**
- **any bleeding from your gums or nose**
- **severe headache**
- **dizziness**
- **an increase in weakness**
- **pain in joints and muscles**

REMEMBER

Even in the absence of piastrinopenia, some targeted therapies (especially those with antiangiogenetic activity) can cause bleeding at different levels with different consequences, such as:

- more abundant menstrual flow
- small red spots under the skin
- bleeding from your gums or nose

In this case, other drugs should be avoided, because they may increase the risk of bleeding (eg aspirin).

In case of haematological toxicity all the above mentioned precautions should be pursued until the values has been recovered. Once recovered the normal values is not necessary to continue with these precautions.

How to cope with the haematological toxicity

ANEMIA: if your red blood cell count falls too low, you may need a blood transfusion and/or treatment (vials mostly to be injected subcutaneously) with growth factors to boost your bone marrow's red blood production.

How to cope with symptoms related to anemia?

- allow time during the day for periods of rest
- limit your daily activities. Do only the things that are most import to you. Ask family, friends and neighbour to pitch in with activities, such as child care, shopping, hose work or driving
- talk with your doctor or nurse about a program of regular exercise
- eat a well-balanced diet (not just eating more red meat you will raise your blood red!) and drink plenty of liquids
- get up slowly to help prevent dizziness after sitting or lying down

LEUCOPENIA (NEUTROPENIA): if your white blood cell count drops too much, your doctor may postpone treatment, or give you a lower dose of therapy, or prescribe a preventive antibiotic therapy (i.e. to prevent a possible infection) and/or therapy (vials mostly to be injected subcutaneously) with growth factors that boost white blood cell production in the bone marrow.

Useful suggestions in case of leucopenia/neutropenia

- Wash your hands often during the day (especially before your meals and after you use the bathroom)
- stay away from people who have infections (colds, flu, measles, etc.)
- avoid crowds (cinemas, public transports, bars, theatres)
- wear gloves when gardening or cleaning up animals or your children (e.g. in changing their diapers)
- do not used any medicine that might modify your immune system before consulting your doctor

PIASTRINOPENIA (TROMBOCITOPENIA):): in some cases your doctor prescribe one or more transfusions of platelets. Currently there are no commercially platelet growth factors, namely drugs that can help the bone marrow to produce more platelets.

Useful suggestions in case of piastrinopenia/thrombocytopenia

- use an extrasoft toothbrush to clean your teeth
- if you need to blow your nose, do it gently into a soft tissues
- take care not to cut yourself when using scissors, knives, needles or tools

- be careful not to burn yourself when ironing or cooking
- avoid contact sports and other activities that might result in injury
- use an electric shaver instead of a razor

- don't cut or tear the cuticles around nails
- don't squeeze or scratch pimples

3. Fatigue

The causes of fatigue are manifold as it can result from disease, anemia (see page 9), targeted therapies or depression due to the disease. It is a disabling event as it prevents to perform daily activities.

Symptoms related to fatigue:

- **feeling of power lack**
- **irritability and sadness**
- **drowsiness**
- **reduced care of his own appearance**
- **decline in sexual desire**

Fatigue is often transient
if related to the treatment and it may improve
or disappear with dose reduction
or discontinuation of the treatment,
to be agreed with your doctor.

USEFUL ADVICES

- limit your activities:
  do only things that are more important to you
- arrange these activities during a whole day,
  rather than in a single moment of it
- choose a healthy diet and drink at least 1.5 litres of liquids during the day
- follow few simple exercises and relaxation techniques
- relax with music or reading a book
- ask family and friends to help you in your daily activities

4. Diarrhoea

Since most of targeted therapies are taken by mouth, diarrhoea is a possible and quite frequent side effect.

Diarrhoea is:

- **more bowel movements than you usually have**
- **stools that are more loose, soft or watery than usual**

It may be associated with abdominal cramps.

REMEMBER

- The diarrhoea may appear immediately after starting the treatment or after several days. Usually it regresses a few days after the drug discontinuation.
- Targeted therapies are NOT the only possible cause, since the combined chemotherapy may be responsible, as well as anxiety, the excessive ingestion of some foods and/or drinks and viral or bacterial infections developed by the gastrointestinal apparatus.

Diarrhoea should be reported to your doctor (note the bowel habit and the frequency of the discharges making a comparison with your usual bowel habit just before you started the treatment with targeted therapy) to avoid dehydration and/or excessive loss of weight.

In some cases, the diarrhoea can lead to an interruption of targeted therapies and/or a dose reduction of them: the doctor assesses the scale and decides the measures to adopt.

WHAT TO DO

- eat smaller amount of food, but eat more often

- after each discharge clean up the anal area with mild soap, rinse with warm water and dry thoroughly

- food and drink at room temperature (neither too hot nor too cold)

- drink 6-8 glasses of non-carbonated drinks to replace those you have lost through diarrhoea (water, apple juice, peach juice, apricot juice, orange juice, clear broths, green tea, ginger ale, Gatorade or similar)

- eat foods rich in potassium such as bananas, oranges, apricots, peaches, potatoes

- choose simple food and not very elaborate (rice, vegetable soups, fruits and vegetables without skin, fish, chicken and turkey, eggs, yogurt)

WHAT TO DO NOT

- avoid coffee (or drinks with caffeine), tea, alcoholic beverages

- avoid spicy, fried or greasy foods
- avoid milk and milk products

- avoid high-fiber food such as broccoli, white bread, cabbage, cauliflower, beans, cereals, bran, raw fruits and vegetables and/or with the skin

- avoid chocolate

Therapy to counter the diarrhoea (it should be agreed with your doctor)

- **You should need milk enzymes to replace the intestinal bacterial flora**
- **In some cases your doctor prescribes loperamide and indicates the method of recruitment. This scheme could be useful in case of prescription of loperamide:**

FIRST DOSE	DURING THE DAY	DURING THE NIGHT
		
Take 2 caplets (4 mg) of loperamide	Take 1 caplet (2 mg) of loperamide every 2 hours	Take 2 caplets (4 mg) of loperamide at bedtime and 2 caplets every 4 hours until morning (if necessary you must set up an alarm clock to wake up during the night to take your tablets)

Stop taking loperamide when you have not had any bowel movements for 12 hours.

5. Skin toxicity

The skin toxicity is a fairly common side effect with targeted therapies (especially for those therapies with **antiepithelial growth factor** activity, but not only). The cutaneous toxicity can appear in different ways in terms of importance and type.

This toxicity could be serious in few cases, but even if moderate it can be very annoying and affect (as visible) your life and the relationships with people. It is important to discuss with your doctor and the nurse to adopt the appropriate measures.

Among the main toxicities of this class:

- **dry skin (and itchiness)**
- **rash**
- **nail toxicity**
- **hand and foot syndrome**
- **discoloration**

Dry skin

USEFUL ADVICES

- avoid hot baths and long showers, using neutral detergent and adding oil to your bath
- use a mild soap to wash the affected area
- after your bath (and often during the day) remember to apply a moisturizing mild alcohol-free cream

- avoid prolonged sun exposure and always use a sunscreen of SPF15 or higher (preferably containing zinc oxid or titanium dioxide) in the exposed areas of your body (face, neck, extremities)
- it can be useful to use: oatmeal colloidal lotions, aloe, glycerine
- use anti-dandruff shampoo to alleviate the discomfort to the scalp
- use large and comfortable clothes and when it is possible, with cotton in contact with the skin
- protect your skin from cold and wind

- maintain a good hydration, introducing at least 1.5 litres of liquids during the day

Itch

USEFUL ADVICES

- apply cold compresses (including ice in a plastic bag wrapped in a towel)
- keep nails short and well-treated (to avoid scratches)
- try to wipe/dab the skin rather than scratch

- change the sheets every day and do not put too many blankets over your bed
- menthol talc on your limbs, stomach and back can give you relief

There are drugs that can relieve the itching, but it is necessary the advice and the prescription of your doctor.

Skin rash

The skin rash usually occurs in the earliest days of therapy. It can appear as:

- **redness with slight flaking skin around the eyebrows and the hairline**
- **it frequently appears on your face, upper chest and back**
- **it may show as redness and then develop the pin white raised**
- **in some cases it may regress leaving that part of the skin discolored**

USEFUL ADVICES

- all measures adopted for the dry skin can also be useful for the rash
- do not shave every day and use the electric shaver instead of a blade
- remove any dermatologist-approved make-up with a gentle liquid cleanser
- it could seems acne, but it is NOT, so avoid over-the-counter acne-related treatments, including products with benzoyl peroxide

There are medicated creams for this side effect and in selected cases your doctor may prescribe an antibiotic medicament also.

Nail toxicity

Targeted therapies may cause nail toxicity, namely inflammation, pain, redness of the nail bed.

USEFUL ADVICES

- it is important to cut carefully and evenly the nails, and if possible, apply a beautician for a regular manicure and pedicure
- do not to use tight shoes and put on your skin cotton socks

There are creams for this side effect and in selected cases your doctor may prescribe an antibiotic medicament, but these approaches must be evaluated and agreed with your him.

Hand-foot syndrome

Hand-foot syndrome is associated with some targeted therapies and usually appears during the first weeks of treatment. If reported to your doctor, usually it is treated without need to stop the ongoing treatment.

HOW TO RECOGNIZE THE HAND-FOOT SYNDROME

SERIOUSNESS	SYMPTOMS ONE OR MORE COMBINED	IMPLICATION ON EVERYDAY ACTIVITIES
slight	• Numbness • Feeling of discomfort in touching objects • Burning or stinging sensation • Tingling • Non-painful swelling • Hands and/or feet redness	• None of these symptoms affect normal daily activities
moderate	• Sore redness • Swelling • Thickening hands and/or feet cute	• Symptoms create discomfort, but do not prevent from carrying out normal daily activities
severe	• Desquamation or exfoliation • Open wounds • Vesicles formation • Skin thickening • Strong pain in hands and/or feet	• Severe discomfort that makes impossible to work and perform normal daily activities

USEFUL ADVICES

- avoid standing up long
- use comfortable large plant shoes and cotton socks
- soak the affected skin in warm water and add magnesium sulphate
- spread on your feet emollient creams or lotions even twice a day
- at night make a lotion or cream compress and wrap your foot in a comfortable cotton sock
- if you see callosities on your feet (or thickening skin) apply the beautician for a pedicure
- excess callused skin may be trimmed down; preparations such as Lachydrin or urea creams offer formulations that help reduce thickened callus skin

Discoloration

Some targeted therapies may cause hair depigmentation, which can also appear different in texture and fragile. The discontinuation of therapy causes a normal color hair growth and the possible resumption of the treatment may cause the discoloration again, so that the hair may seem like "a band".

These color alterations can also appear on the skin and on some fluids (i.e. urine) and secretions. Some targeted therapies give to the skin a yellowish color, regressing with the discontinuation of treatment.

This toxicity should not scare because it has no clinical aspect; in any case it should be reported to the doctor.

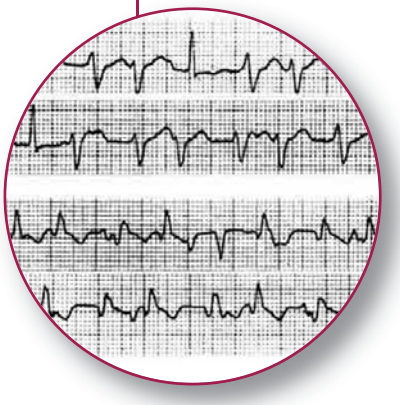
6. ECG alterations

Targeted therapies may cause ECG alteration, in absence of signs or symptoms in patients receiving this treatment. For this reason, in the first period of treatment, and also later, your doctor may ask you to repeat this test several times (even at close range between a test and the other), with defined deadlines.

ECG is not a painful examination, it does not involve any risk and it is rapid to perform.

In case of ECG alterations your doctor considers the opportunity to suspend and/or reduce the targeted therapies.

These ECG alterations (actually in a very small percentage of cases) may cause an abnormal heart rhythm (i.e. a variation of the heart beats in terms of number and kind of beats per minute).



7. Endocrinological abnormalities

Some targeted therapies may cause an altered function of certain glands (**endocrinological abnormalities**), such as the thyroid. For this reason your doctor makes, if necessary, specific blood tests to assess this function, before and during therapy. A reduced function of thyroid gland (hypothyroidism) is possible in less than 5% of patients receiving targeted therapies and regresses after the treatment cessation or with an appropriate therapy (based on thyroid hormones) that your doctor prescribes, if necessary.

In most cases, hypothyroidism is initially asymptomatic and is detected by performing blood tests.

The symptoms that may underlie a condition of hypothyroidism (they should be reported to your doctor) are:

- **decline in sexual desire (it can also refer to the stress condition related with cancer)**
- **cold feeling**
- **depression**
- **daytime sleepiness (although you have rested during the night)**
- **dry and brittle hair**
- **concentration difficulty**
- **constipation**

8. Loss of appetite

At the base of the loss of appetite there may be several reasons including difficulty in swallowing, nausea and vomiting, taste alteration, but also fatigue and depression.

It can begin with the refusal of the favourite foods and may also involve the loss of weight.

USEFUL ADVICES

WHAT TO DO

- Eat only the amount of food you desire
- Think that food is an integral part of the treatment

- Make **small meals or snacks*** throughout the day whenever you want. You don't have to eat three regular meals each day

- Change your mealtime routine.
  For example, eat by candle-light or in different location
- Try new foods and more foods

- Eat with friends and/or with the family or with the radio or television on

- Take a walk before meals whenever possible. This may make you feel hungrier

- Eat foods high in calories, easy to eat, such as puddings, ice creams, smoothies and yogurt

- Drink between meals rather than during the meal
- Eat fresh foods or at room temperature

* IDEAS FOR SMALL SNACK (SEVERAL TIMES DURING THE DAY)


Apple juice


Snacks, muffins, plum-cake and crackers


Slices of cake or biscuit (also with added fruit among the ingredients)


Cereals, muesli


Milk chocolate


Creamy soups


Dried fruit (raisins, prunes or apricots)


Fresh fruit


Pizza


Sandwiches


Ice cream


Yogurt


Juice or fruit cream


Milkshakes


Vegetables (carrot/celery/radish)


Cheese (fresh or parmesan)


Eggs (e.g. boiled)

If the inappetence persists it may be useful to take protein dietary supplements and in some cases it is important to resort to a dietician.

9. Nausea/Vomiting

Some of targeted therapies may be responsible for nausea and vomiting, after the first few days of therapy, or even after several days of treatment.

Nausea and vomiting depends on different factors, including on the drugs you are receiving, on your individual response and on your psychological and emotional state.

If nausea and vomiting appear ONLY when you go to the hospital for visits and tests, indicating your anxiety and fear for news on your disease and/or therapy and the results of examinations, the best way to handle this anticipatory nausea is through anxiolytics (benzodiazepines), always with a doctor's prescription.

There are drugs that help relieve nausea and vomiting (antiemetics). Different antiemetics work for different people. It may be necessary to try more than one before you get relief. Don't give up: continue to work with your doctor and nurse to find the one that works best for you.

TO BE AVOIDED

- Go to bed 1 to 2 hours after the meal
- Force yourself to eat food against his own will
- Eat red meat
- Eat sweet, fried or fatty foods

USEFUL ADVICES

- Try to avoid odors that bother you such as cooking smell, smoke or perfume
- Do not to eat and do not remain long in the same room where foods are cooked
- Tend to drink out of meals and not during the same

- Choose fresh drinks, fizzy and sweet
- Choose white meat

- Avoid big meals so your stomach won't feel to full. Eat frequent small meals throughout the day instead of one, two or three large meals (see tips on snacks pag. 25)
- Chew your food well and slowly for easier digestion
- Eat foods at room temperature (avoiding foods and drinks too cold or too hot)

- Suck on ice cubes
- Rest in a chair after eating, but don't lie flat for at least two hours after you've finished your meal
- Usually the morning is the best time for well-being: in this case it is advisable have a breakfast with high nutritional content
- Breathe deeply and slowly when you feel nauseated
- Wear comfortable shoes and clothes

- Use relaxation techniques: ask your doctor about programs near to your home

10. Hypertension

Hypertension is an abnormal increase of blood pressure. Blood pressure is the energy through which the blood circulates in the arterial vessels. The values of blood pressure varies depending on the age, tending to increase over the years, and during the day, resulting highest on awakening, tending to decrease during the day, increasing in the case of physical and emotional stress. It is understandable that there are not in absolute normal values of blood pressure and the net limits setting can appear arbitrary.

Some of the targeted therapies (particularly the **antiangiogenetic**) can cause hypertension compared to the previous values at the beginning of therapy or a congestive pressure in patients already treated for hypertension (i.e. patients with a diagnosis of hypertension prior the start of targeted therapies treatment, for which, the antihypertensive therapy maintained normal blood pressure).

According to the treatment agreed with your doctor, you will be shown if to measure blood pressure and how often. Usually weekly assessments or fortnightly are sufficient.

Hypertension usually occurs early in the course of treatment.

In the case of hypertension, your doctor prescribes one or more appropriate medications (anti-hypertensive) or sets again your antihypertensive therapy in the case you suffer from hypertension before starting this therapy.

USEFUL ADVICES

- control your body weight
- avoid alcoholic drinks
- do not abuse of licorice (avoid licorice candies)
- try to do some movement: at least one walk a day, when possible
- try to eat foods high in magnesium and potassium such as bananas, cereals, fresh fruits and vegetables, citrus fruits
- reduce the salt and foods rich of it (i.e. sausages, see also table “diet low in salt”*)
- choose steam or grill cooking, foil in the oven and low fat cooking

*DIET POOR IN SALT

Recommended foods	Not recommended foods
 Bread without salt	 Tuna or other canned fish (anchovies, herring)
 Rice	 Ham, sausages
 Fresh cheeses	 Aged cheeses
 White meat and fish	 Sauces (mayonnaise, mustard, ketchup)
 Vegetables	 Butter
 Fresh fruit	 French fries
 Cereals	 Stock cube
 Yogurt	 Alcohol
 Olive oil	

11. Thromboembolic events

Some targeted therapies can increase the risk of forming clots (small "plugs") into the venous vessels (or arterial) where the blood flows. Remember that cancer may increase the thrombotic risk.
Embolization is the detachment of small fragments (small clots of blood) of thrombi from the place where they are formed, which localize in other blood vessels. Embolization is a very rare consequence of a thrombotic event.

Most commonly the thrombotic event affects the superficial or deep venous circle of upper or lower arts (i.e. arms or legs).

The signs of a venous thrombosis are:

- **pain in the affected area**
- **redness**
- **swelling vein (visible only if superficial)**

USEFUL ADVICES

- to prevent thrombotic events the movement is essential. Even sitting in the armchair try to do small exercises (for example, by sliding a rolling pin under your feet back and forth)
- avoid remaining long stand up or still in the same positions
- avoid long hot baths

12. Glossary

Angiogenesis (neo-angiogenesi): formation of new blood vessels that cancer cells need in order to grow.

Antiangiogenetic: acting “against” new blood vessels formation.

Blood vessel: a tube through which the blood circulates in the body. Blood vessels include a network of arteries, arterioles, capillaries, venules and veins.

Endocrinology: it is the part of medicine studying internal secretion glands, namely those whose product is directly injected in the blood. These products are called hormones.

Enzyme: a protein that speeds up chemical reactions in the body.

Epithelial growth factor (epithelial growth factor): growth factor (i.e. factor able to stimulate the proliferation and refinement of the cell) present on the normal and tumor cells surface (being more and more active on tumor cells).

Protein: a molecule made up of amino acids that are needed for the body to function properly.

WALCE Onlus (Women Against Lung Cancer in Europe)
is a non-profit organization created to make women aware
of the significant increase of lung cancer in women.
WALCE aims to spread knowledge of this disease in terms of prevention,
diagnosis and therapy.
WALCE was founded in 2006 as an Italian-Spanish initiative.
It aims to be the first association to function on a European scale
in the fight against lung cancer.
This is the disease which is difficult and complicated to treat and in which women
play a leading role on a daily basis, whether they are doctors, nurses, patients,
family members or caregivers.
Women are often a point of reference and a source of support and hope.

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