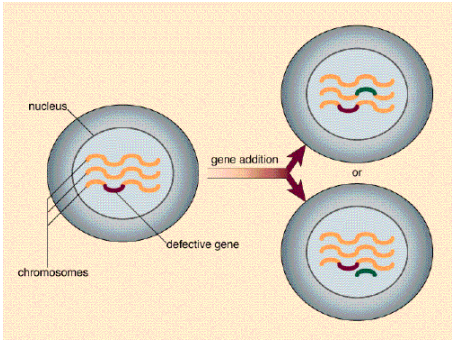
Gene therapy Case studies

2020

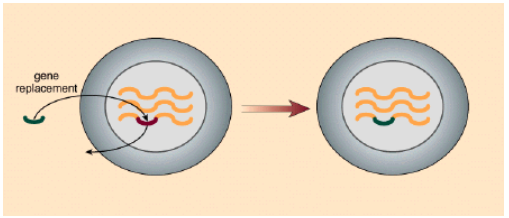
Gene Therapy The Principles

Molecular Strategies

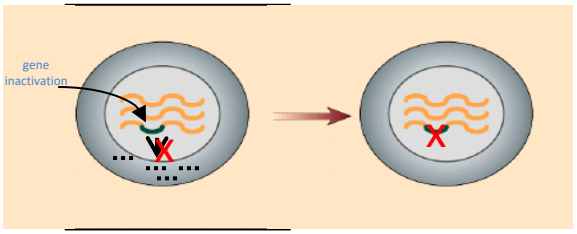
1- Gene augmentation/addition



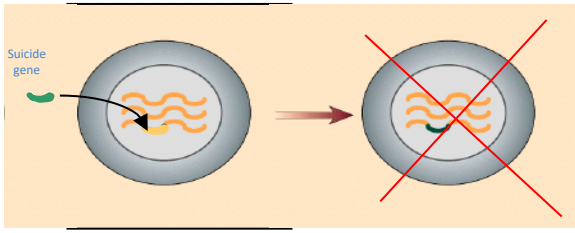
2- Targeted mutation correction



3- Targeted inhibition/inactivation of gene expression

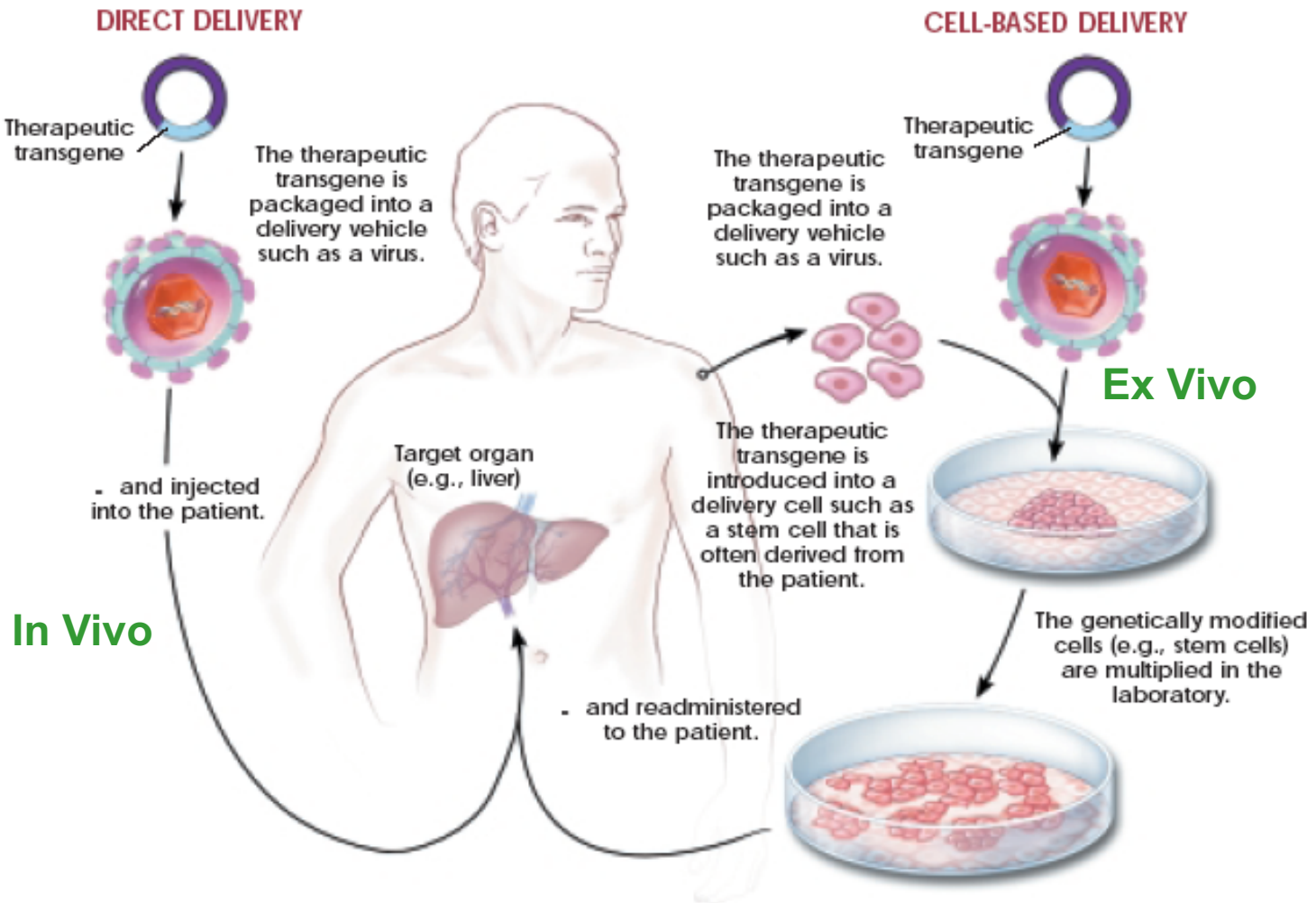


4- Targeted killing specific cells



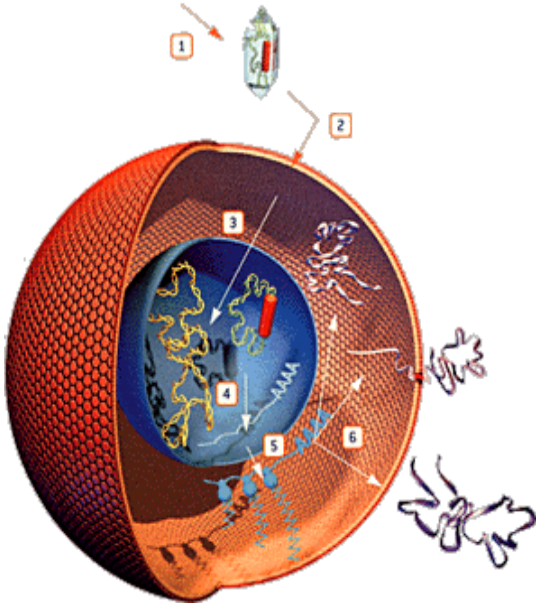
Gene therapy principles

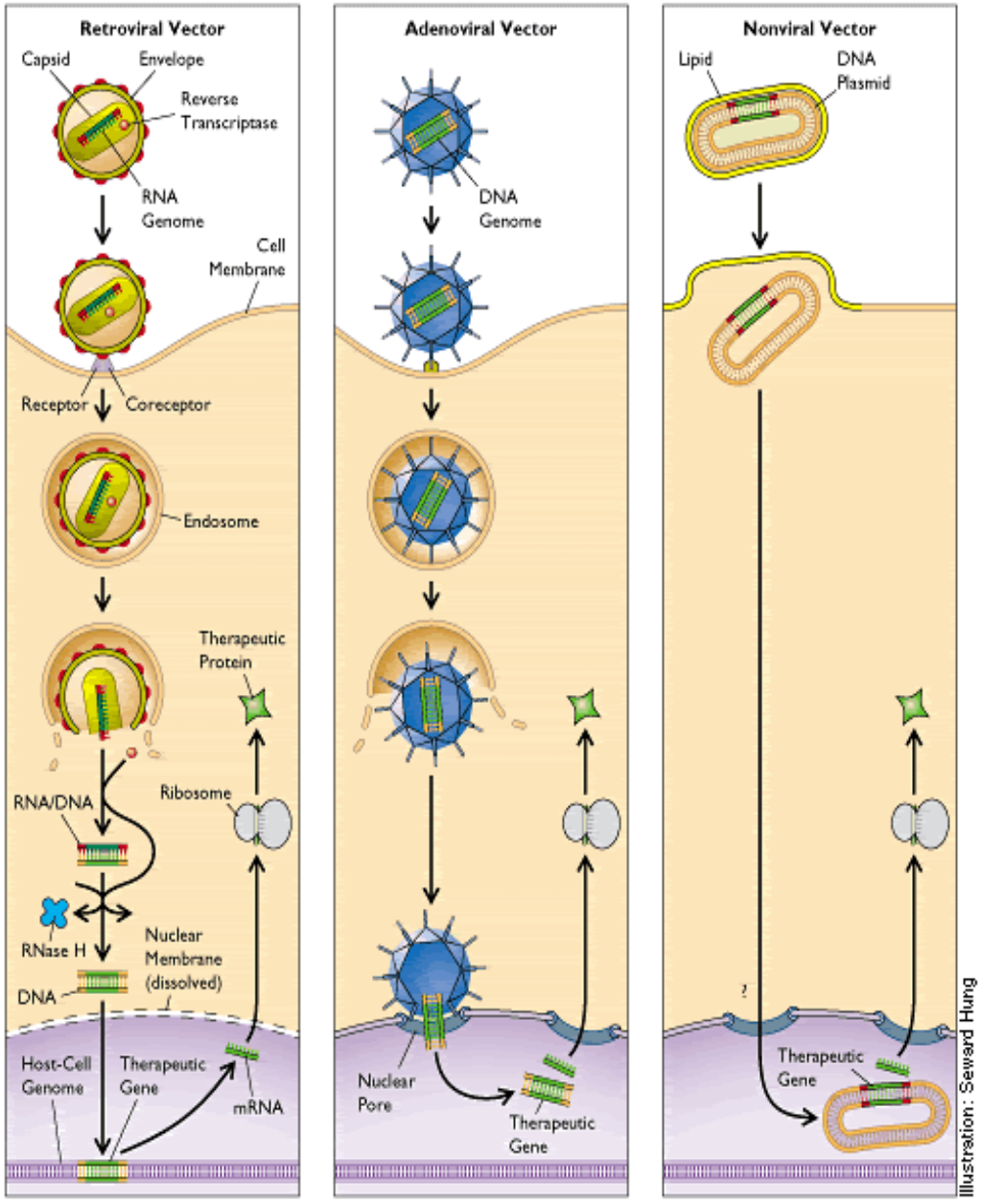
gene transfer modes



Gene therapy Vectors

Therapeutic Gene + Vector





1- Place the Transgene on the vector

2&3 – The vector transports the Transgene into the cell and into the nucleus

4- The Transgene is transcribed to mRNA

5&6- The Transgene is translated into a protein that could be intracellular ou secreted

Assignment

1- How would you treat the patient. What molecular strategy?

2- Which therapeutic gene would you use and/or target?

3- How would you apply the therapy?

4- What would be the expected outcome (clinical end-point)?

Assignment

Consider the following patients:

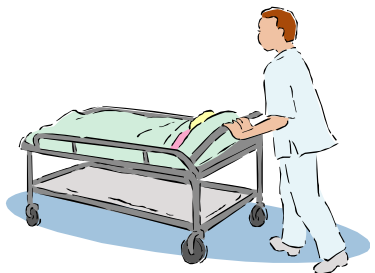
Patient #1:

Symptoms

In the infant's first few months of life, parents notice a lack of visual responsiveness and roving eye movements, known as nystagmus. She is now 18 months and often pokes, presses, and rubs his eyes. An electroretinogram (ERG) detected little activity in the retina.

Diagnosis: Leber congenital amaurosis

It is a group of inherited retinal diseases characterized by severe impairment vision or blindness at birth. Clinical genetic diagnoses revealed mutations in both copies of the RPE65 gene.



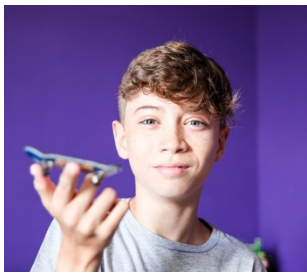
Assignment

Consider the following patients:

Patient #2:

Symptoms

Showed at early age anemia and frequent infections. At the age of 8 started to show weakness and fatigue. He showed delayed growth. At 16 he started to receive blood transfusions.

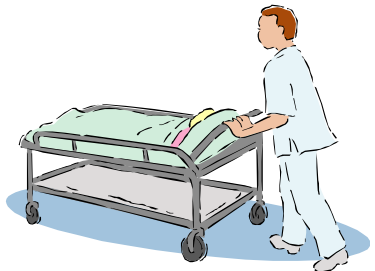


Diagnosis: Beta thalassemia

Rare, inherited disease blood disease characterized by a reduced of ß-globin, a component of an oxygen-carrying protein called hemoglobin. ß-thalassemia is caused by mutations in the beta-globin (HBB) gene.

Notes:

No HLA matching donor for bone marrow transplantation
Reasonable stem cell pool in bone marrow



Assignment

Consider the following patients:

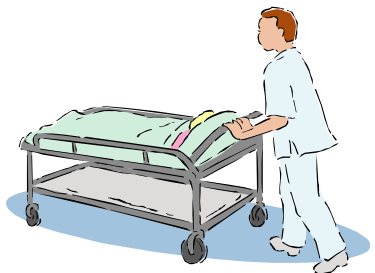
Patient #3:

Symptoms

Enlarged lymph node on the outside of the neck, a sore throat and a hoarse sounding voice. Painful swallowing observed at the age of 58.

Diagnosis: Oral Cancer (Head and neck cancer

Cancer that start in the upper aerodigestive tract including the lip, oral cavity (mouth). It spread to the lymph nodes of the neck showing the first sign of the disease.



Answers

Assignment

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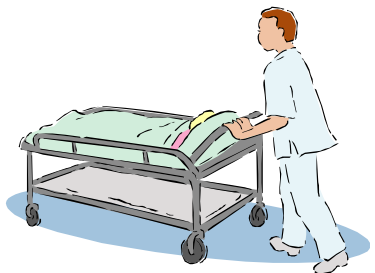


Assignment

Patient #1:

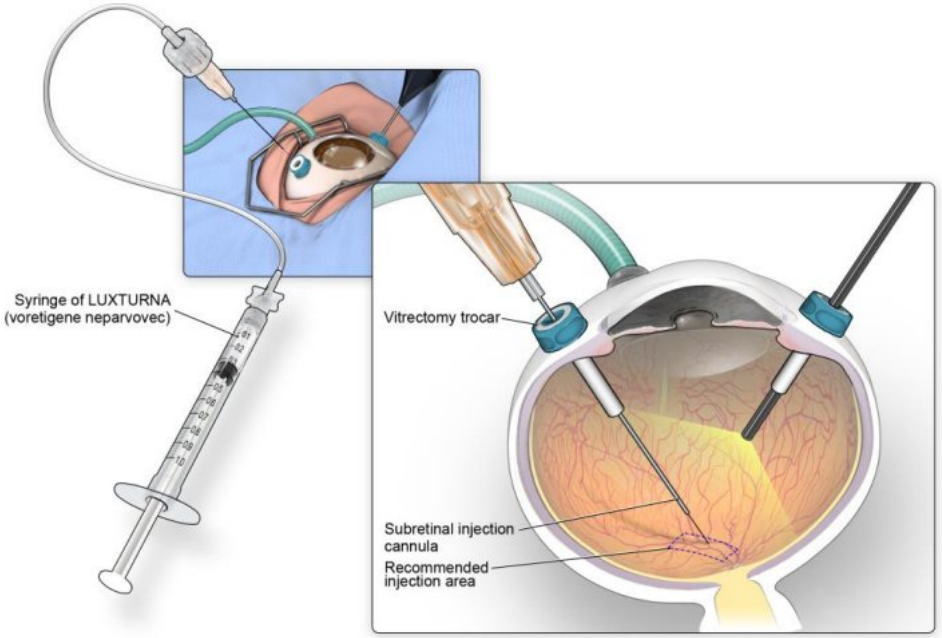
Diagnosis: Leber congenital amaurosis

mutations in both copies of the RPE65 gene.

LUXTURNA is a prescription gene therapy product used for the treatment of patients with inherited retinal disease due to mutations in both copies of the *RPE65* gene, which can only be confirmed through genetic testing.

LUXTURNA™
voretigene neparvovec-rzyl
for subretinal injection

2017



Assignment

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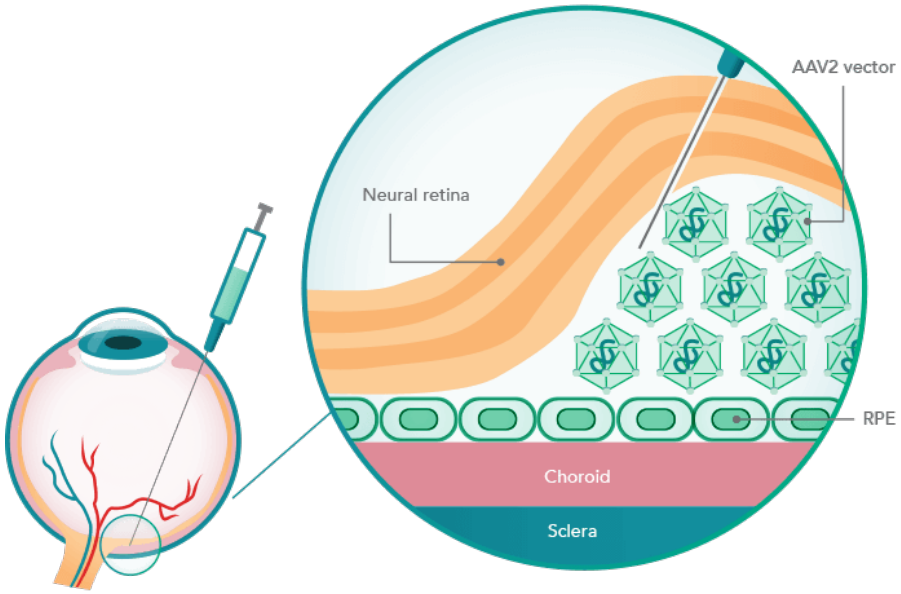
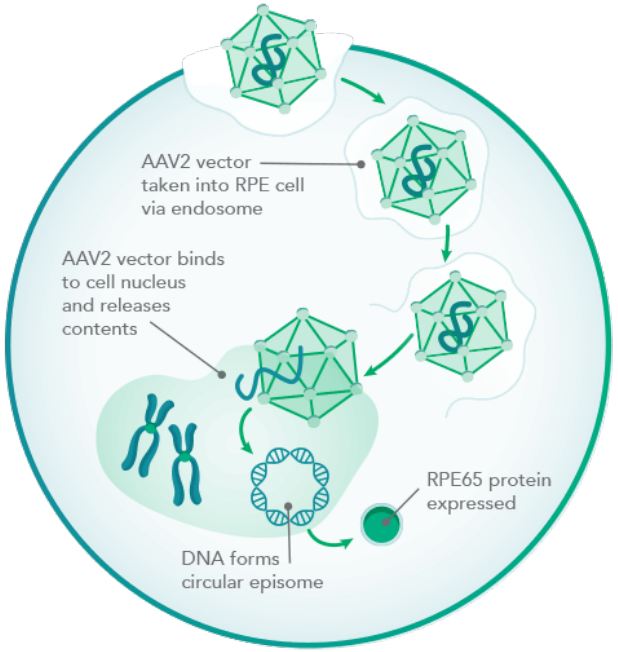
Diagnosis: Leber congenital amaurosis

mutations in both copies of the RPE65 gene.

LUXTURNA is administered via subretinal injection following a vitrectomy





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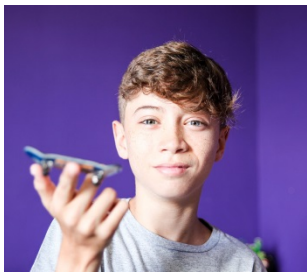

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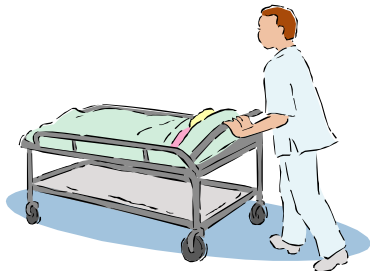


Assignment

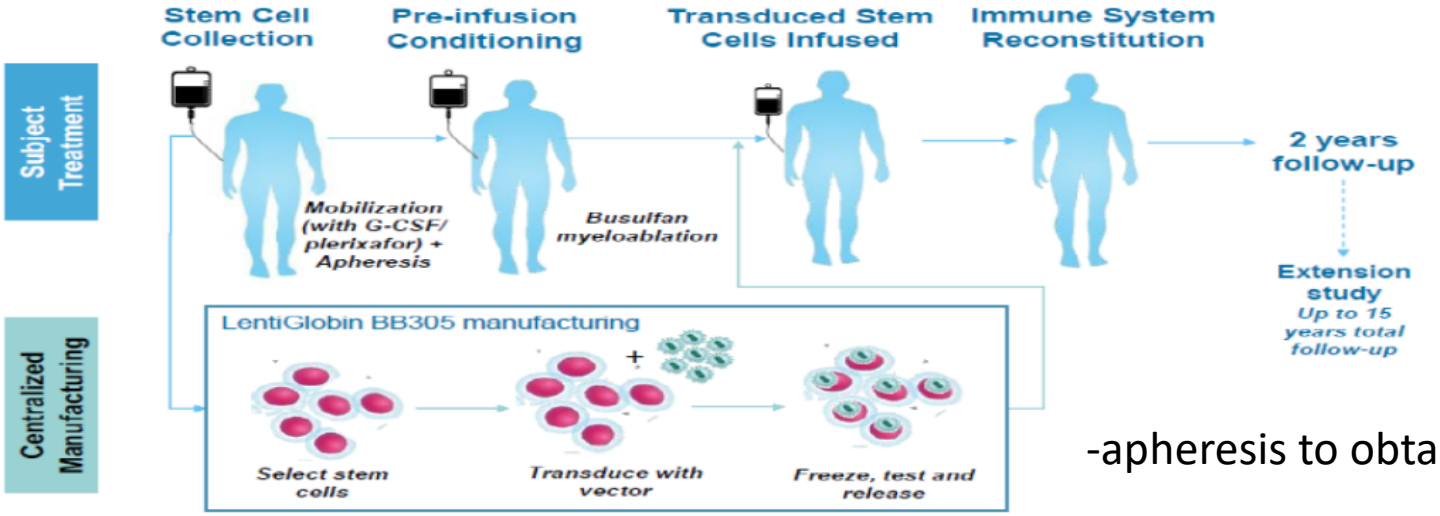
Patient #2:

Diagnosis: Beta thalassemia

mutations in the beta-globin (HBB) gene.

- **Zynteglo - LentiGlobin™** – Bluebird (U.S.A.)

  - gene therapy drug for the treatment of β-thalassemia (severe sickle cell) . LentiGlobin BB305 is a lentiviral vector which inserts a functioning version of the HBB gene into a patient's blood-producing hematopoietic stem cells (HSC) ex vivo. The resulting engineered HSC cells are then reintroduced to the patient.



-apheresis to obtain CD34+

Autologous CD34+ hematopoetic stem cells transduced w/ human beta-globin gene
Administration: min dose of 7.80 × 106 CD34+ modified cells/kg as an intravenous infusion

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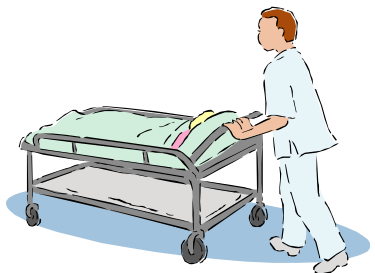


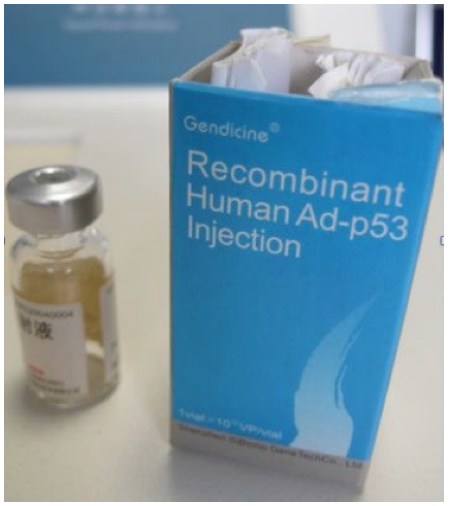
Assignment

Patient #3:

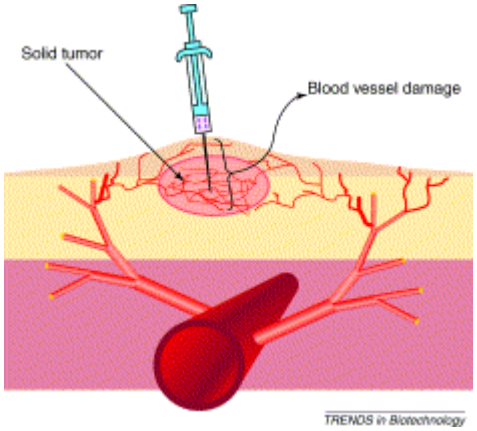
Diagnosis: Oral Cancer (Head and neck cancer

- **Gencidide –** SiBiono GeneTech Co. (China)

  a p53 adenovirus for the treatment of head- and neck squamous cell cancer (is used in combination with radiotherapy)



Route of application: CFDA-approved route of administration for Gendicine is intratumoral injection, and this is therefore the most widely applied method.



For some cancers in which cancer cells are widespread, or for patients with metastases, direct intratumoral injection is not applicable, various routes of application, including arterial injection, intraoperative, intra-tract (bronchial, esophageal, intra-cavity, or systemic infusion, have been applied according to the patient's condition in order to improve gene delivery efficiency.