Vaccines:

Bacillus Calmette Guerin (BCG; TheraCys)

Uses: Superficial bladder cancer; administered intravesically (directly into the bladder). Administered repetitively through an induction phase (once per week for 6 weeks), then in a maintenance phase at 3, 6, 12, 18, and 24 months following the first dose.

Mechanism: The BCG vaccine is made from a live, but attenuated bacterium strain (*Mycobacterium bovis*) which is related to human tuberculosis (TB) bacteria. The exact mechanism is not known, but when administered intravesically as a cancer therapy, BCG promotes a local acute inflammatory and sub-acute granulomatous reaction with macrophage and lymphocyte infiltration in the urothelium of the urinary bladder.

Toxicities: Dysuria, urinary frequency, hematuria, fever.

Note(s): BCG was developed as a vaccine against mycobacterium tuberculosis (MTB) and is still used in some parts of the world. Its effectiveness against MTB is controversial.

Sipuleucel-T (Provenge)

Uses: For early (asymptomatic or minimally symptomatic) metastatic castrate resistant prostate cancer, also called hormone refractory prostate cancer.

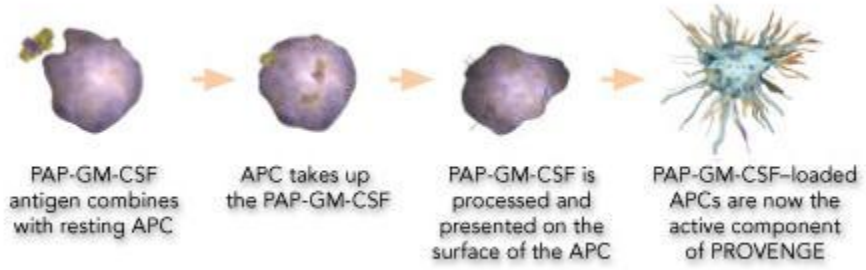
Mechanism: Classified as an autologous cellular immunotherapy and designed to induce an immune response targeted against PAP (prostatic acid phosphatase), an antigen expressed in most prostate cancers. See Figure 1.

STEPS: (1) Obtain blood cells from patient via standard leukapheresis 3 days prior to reinfusion date. (2) Ship the cells to a special facility, and then in culture expose the cells to PAP-GM-CSF (PAP linked to GM-CSF). APCs take up and process the recombinant target antigen into small peptides that are then displayed on the APC surface as a consequence of stimulation by GM-CSF. (3) Ship the activated cells (sipuleucel-T) back to the patient's clinic and then re-infuse.

Toxicities: Serious but rare acute infusion reactions, cerebrovascular events. More common adverse events include chills, fatigue, fever, back pain, nausea, joint ache, and headache.

Note(s): Because the therapy is an autologous cellular immunotherapy, each batch of the vaccine is actually somewhat different for each patient.

Figure 1. Activation of antigen presenting cells to generate sipuleucel T (Provenge).



Gardasil

Uses: Protection from infection by human papilloma viruses (HPV); administered by injection as 3 doses (at 0, 2, and 6 months). Approved for females and males ages 9-26.

Mechanism: Targets two high risk HPV viruses (HPV-16 and HPV-18). HPV is known to cause cervical intraepithelial neoplasia (CIN) which is a precursor to cervical cancer. Also targeted against HPV-6 and HPB-11 that can cause genital warts.

Toxicities: Most are considered non-serious (e.g., fainting, pain and swelling at the injection site (arm), headache, nausea and fever). Fewer (<10%) are serious (death, permanent disability, life-threatening illness and hospitalization). There is no proven causal link between the vaccine and serious adverse effects; all reports are related by time only. However, they must be considered "related" to drug administration because the effect happened some time after the vaccination.

There are also rare reports of a disorder called Guillen Barre Syndrome (GBS) occurring after the vaccinations. GBS causes muscle weakness. There is no evidence suggesting that Gardasil causes or raises the risk of GBS. Finally, there have been rare reports of blood clots forming in the heart, lungs and legs.

Note(s): HPV is the most common sexually transmitted infection in adults in the world. Furthermore, it is estimated that most adults will have contracted at least one strain of HPV by age 50.

Cervarix

Uses: Like Gardasil, protection from infection by human papilloma viruses (HPV); administered by injection as 3 doses (at 0, 1, and 6 months). Approved for females ages 10-25.

Mechanism: Targets two high risk HPV viruses (HPV-16 and HPV-18). HPV is known to cause cervical intraepithelial neoplasia (CIN) which is a precursor to cervical cancer. Vaccine also has cross-reactivity to two other HPV viruses (HPV-31 and HPV-45). Finally, it also contains AS04 (3-O-desacyl-4'- monophosphoryl lipid A), an adjuvant that boosts the immune system.

Toxicities: Fatigue, headache, myalgia, gastrointestinal symptoms, and arthralgia.

Note(s): A comparative clinical trial indicates that this agent is superior to Gardasil in terms of immune response to HPV, but does not protect from genital warts.