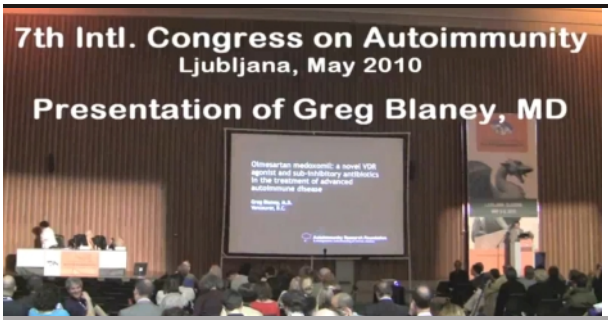
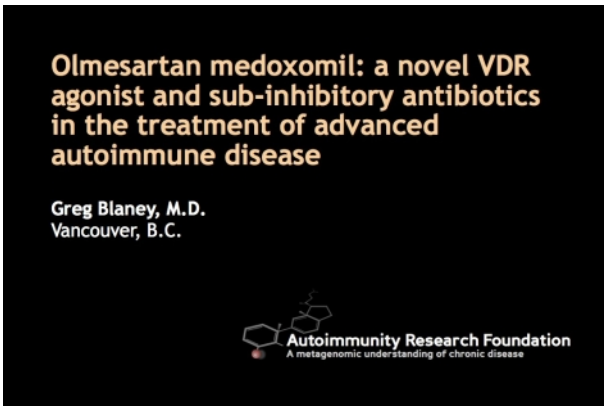


Olmesartan medoxomil and treatment of autoimmune disease

PRESENTED BY GREG BLANEY, M.D.
Vancouver, B.C.

7th International Congress on Autoimmunity
Ljubljana, Slovenia, May 5-9, 2010.
Transcript of video at
http://www.youtube.com/watch?v=X0y0PcVJ5Ss

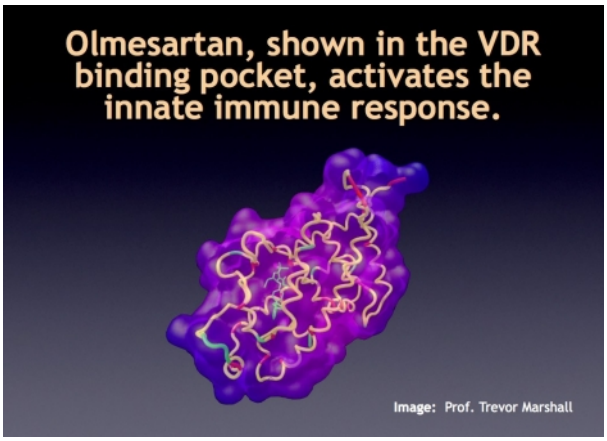
Autoimmunity Research Foundation
A metagenomic understanding of chronic disease
THOUSAND OAKS, CA, USA



Slide 1 [00:00:10]
Greetings.

I will be presenting case studies of three severely ill patients suffering from classical autoimmune disease. Specifically, I will be reporting the remarkable improvements achieved through the stimulation of the immune response.

Stimulating the immune system in autoimmune disease appears counter-intuitive. However, recent research in microbiology has clearly identified the incredible capacity of microbes to persist in the body. This is achieved through a variety of mechanisms, one being the production of ligands that act as antagonists of nuclear receptors.

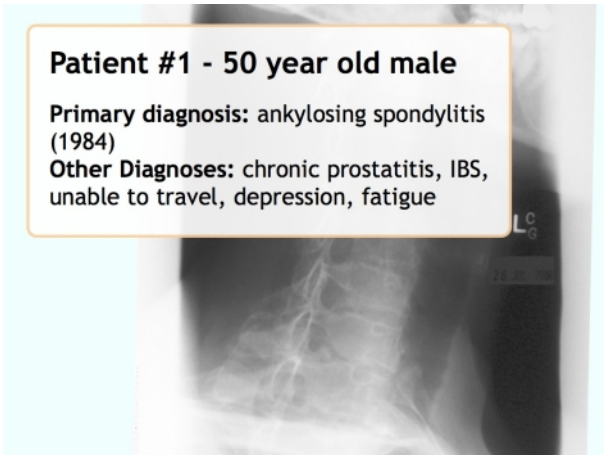


Slide 2 [00:01:00]

Dr. Marshall and his colleagues have shown the presence of VDR resistance in autoimmune disease and that olmesartan is a VDR agonist with high affinity.

The following case studies show the clinical response to an immune stimulation protocol using olmesartan in doses of 40 mg four times per day.

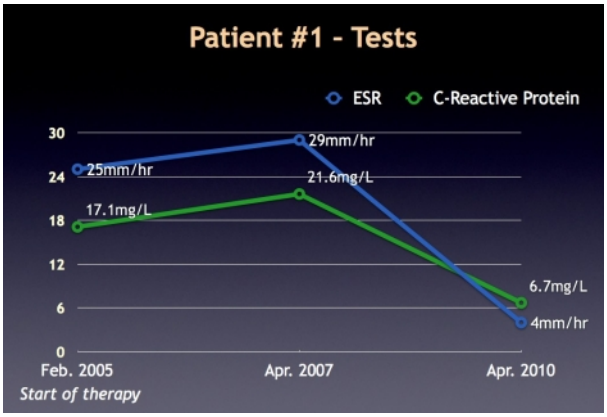
Additional immune stimulation was achieved by the use of low-dose, bacteriostatic antibiotics to inhibit both bacterial virulence factors and quorum sensing signaling capabilities.



Slide 3 [00:01:45]

Case 1 is ankylosing spondylitis in a now 50-year-old male. Onset was at the age of 26, initially as sacroiliitis. It progressed in a typical fashion with increasing rigidity of the spine, fusion of cervical facet joints, pain and fatigue. He also developed co-morbid conditions including chronic prostatitis, neuropathy, irritable bowel syndrome, insomnia, depression and he was unable to work full time.

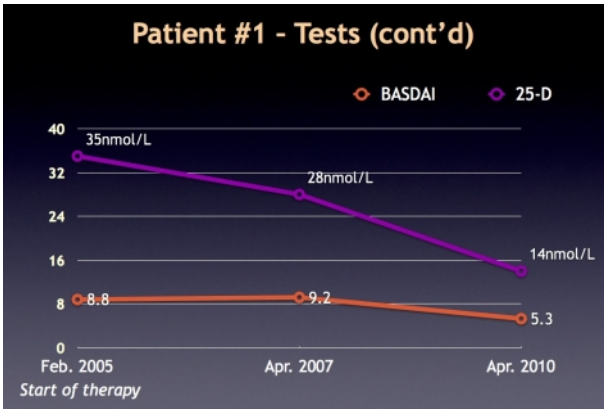
He started treatment December 2005.



Slide 4 [00:02:26]

He experienced waxing and waning of symptoms both physical and emotional through the first 3 years of treatment, peaking in mid 2007.

Presently, he is no longer depressed and is back working full time in international finance. His prostatitis has cleared, as has his IBS. Bone density *increased* 11% in his femur and 5% in his lumbar vertebrae over the last 2 years. And during that time, his 25-D levels were deficient to the point of very deficient, in his last reading which was 14 nmol/L.

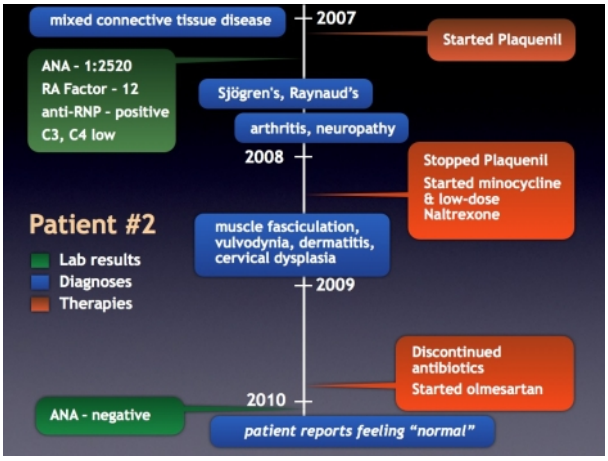


Slide 5 [00:03:06]

His Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], which had risen from 8.8 to 9.2 in mid 2007, is now 5.3. (Previous slide shows 4mm/hr. I hope you know it is per min.)

Slide 6 [00:03:43]

Case 2 is a 37-year-old female who developed autoimmune arthritis two weeks after suffering from a STD. She rapidly deteriorated, developing dry eyes and mouth, Raynaud's, paraesthesia, myalgia, malaise and dermatitis. Her diagnosis changed from reactive arthritis to mixed connective tissue disease.



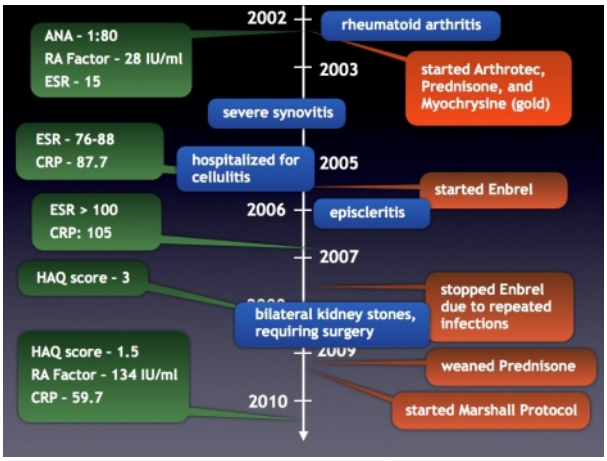
Slide 7 [00:04:10]

As you can see, her ANA was 1:2520 and her anti-RNP was positive. She was on Plaquenil for approximately a year and then she discontinued.

She started olmesartan in October of 2009. She improved rapidly. Today, she states that most days she feel "normal," and only when trying to do physical things does she realizes that she's not 100%. She can walk on the treadmill and do light weights. She still needs eye drops but only on waking. She is back to working full time. Her ANA is negative.

Slide 8 [00:04:51]

Case 3 is 44-year-old male diagnosed with severe and aggressive Rheumatoid Arthritis 8 years ago.



Slide 9 [00:05:03]

Unresponsive to treatment, he was plagued by side effects including recurrent and severe infection—requiring hospitalizations, renal calculi, osteoporosis and massive weight loss. Prior to starting olmesartan, he had been on DMARDs since his diagnosis in 2002. He had been on Arthrotec, Celebrex, Plaquenil, gold injections, Enbrel, Fosamax, calcium, vitamin D and Ibuprofen.

Now, a little more than a year after starting olmesartan, his inflammatory joint disease has diminished significantly. He has regained 25 kilos, and controls pain with low dose Ibuprofen. His Stanford Health Assessment Questionnaire score has fallen from 3.0, in both disability and pain categories, to 1.5.

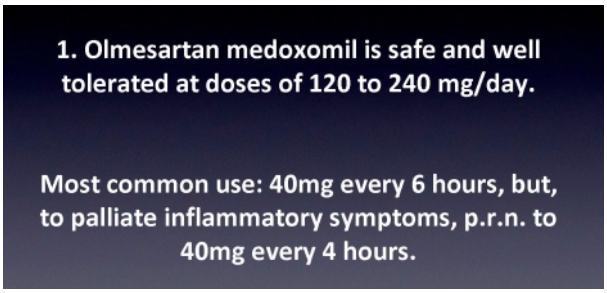
In terms of the immunostimulating effect, if you note at the bottom part of this slide, his RA factor has **climbed** to 134. His CRP has **fallen** to 59.7.

DISCUSSION [00:06:20]

In none of these, or any of the other patients treated, were there any serious side effects or infections.

These 3 cases were selected from a cohort of over 200 patients that I have either treated or collaborated on over the last 5 years. They were selected because they were advanced classical autoimmune disease and they highlighted several important aspects of the treatment.

All had a history of exposure to microbes able to persist prior to onset of their autoimmune disease. Case #1 had severe acne and exposure to Hepatitis B. Case #2 had antibodies to Parvovirus B19 and Chlamydia pneumoniae. Case #3 was antibody positive to Borrelia.



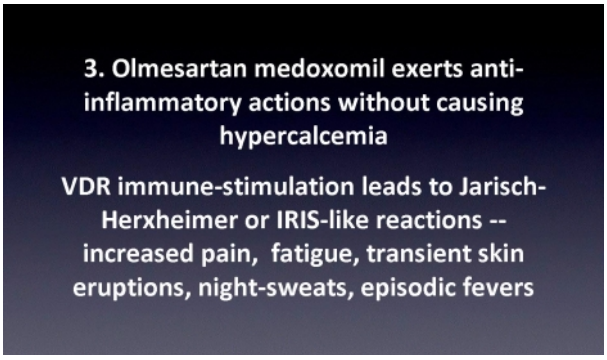
Slide 10 [00:07:08]

What do these and similar results suggest?

First, that olmesartan is safe and well tolerated at doses of 120 to 240 mg per day.

Slide 11 [00:07:29]

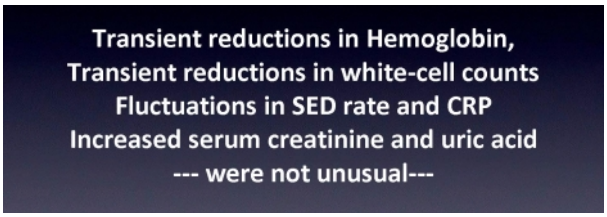
Second, it is an effective anti-inflammatory in autoimmune disease via angiotensin II receptor 1 blockade and VDR agonistic effects.



Slide 12 [00:07:38]

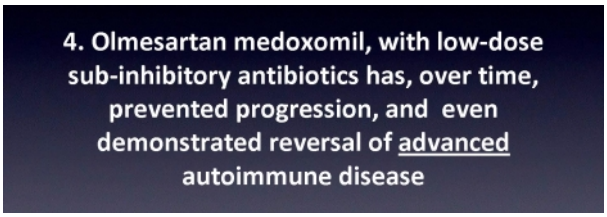
Third, olmesartan is a VDR agonist that does not cause hypercalcemia. Olmesartan induced VDR activation resulted in increased symptoms and changes in clinical markers reflecting immune stimulation.

The increase in immune response leads to apoptosis of infected cells. The increase in released cytoplasmic peptides and increased effector T cell activity causes a combination of Jarisch-Herxheimer and IRIS-like reaction. Increased pain, fatigue, transient skin eruptions, night sweats, episodic fevers were all commonly seen early in the treatment.



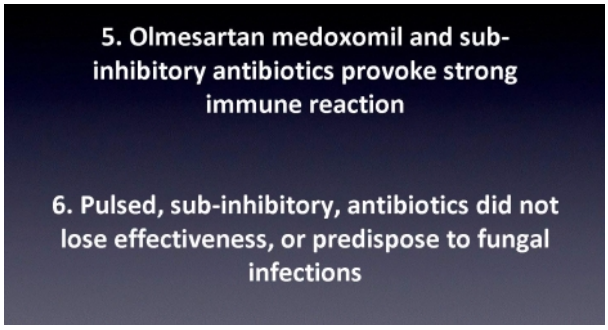
Slide 13 [00:08:26]

Transient reduction in hemoglobin, white cell counts, fluctuations in SED rate & CRP, increased serum creatinine and uric acid were also not unusual. **Serum levels of 1,25-D levels, however, fell**.



Slide 14 [00:08:46]

Fourth, that olmesartan and antibiotics at sub-inhibitory doses can, over time, prevent progression and often even reverse advanced autoimmune disease.



Slide 15 [00:09:02]

Fifth, antibiotics used in this manner provoke strong immune responses, as evidenced by clinical and laboratory reactions.

Sixth, low dose, pulsed bacteriostatic antibiotics, taken over a prolonged time are safe and are not associated with development of bacterial resistance or overgrowth of other pathogens such as C. difficile or Candida albicans.

Slide 16 [00:09:30]

Finally, persistent infection is a likely cause of some autoimmune and chronic diseases that are associated with immune imbalance.

The recognized capacity of bacteria to resist lysosomal degradation, to be able to transform into cell wall deficient forms, to communicate and share information, to create persister cells and the ability to establish biofilms, all enable persistence. Any or all of these actions could then have a profound impact on immune capacity and tolerance. If so, it will explain some of the mysteries still existing in autoimmunity and open up new opportunities for therapy.

Thank you very much.