Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: October 20, 2017

Time: 9:00 a.m. – 2:11 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Conference Room D, Boise, Idaho

Moderator: Phil Petersen, M.D.

Committee Members Present: Phil Petersen, MD-Chair; Tami Eide, PharmD; Christopher Streeter, MD; Paul Driver, PharmD; Perry Brown, Jr., MD; Stephen Carlson, PharmD; Cali Bradberry, PA; David Agler, MD; Andrei Rudyi, PharmD; Berk Fraser, RPh; Joseph Weatherly, DO.

Committee Members Absent: Brian Crownover, MD.

Others Present: Sarah Martinez, PharmD, Magellan Health Services; Jane Gennrich, PharmD, Division of Medicaid; Clay Lord, Division of Medicaid; Ashley Fretwell, Division of Medicaid; Keshia Schneider, Division of Medicaid; Mark England, PharmD, Magellan Medicaid Administration.

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	*Phil Petersen, MD*	Dr. Petersen called the meeting to order.
Committee Business		
➢ *Roll Call*	*Phil Petersen, MD*	Dr. Petersen completed the roll call and welcomed the P&T Committee members.
➢ *Reading of Confidentiality and Mission Statements*	*Phil Petersen, MD*	Dr. Petersen read the Confidentiality and Mission Statements.
➢ *Approval of Minutes from May 19, 2017 Meeting*	*Phil Petersen, MD*	The May 19, 2017 Minutes were reviewed. Apart from correction of a typographical error on page 12, the minutes were accepted as proposed.

Update on Idaho Opioid Equivalent Dosing Project	*Mark England, PharmD* *Magellan Medicaid Administration*	**<u>Update on Idaho Opioid Equivalent Dosing Project</u>** Dr. England provided an update on the Idaho Opioid Equivalent Dosing Project. The Morphine Milligram Equivalence (MME) edit went into effect on July 19, 2017. **Prior Authorization** • Required if a patient exceeds the 90 MME per day threshold for the combination of all short- and long-acting opioids using a calculator based on the CMS standard opioid conversion factors. o PA Requests processed by IDHW Clinical Call Center totaled 160 from 7/19/17 to 10/9/17, with 128 approved and 29 denied (3 requests withdrawn) o Medicaid clinical staff pharmacists can view ▪ The incoming claims that caused the MME quantity limit to be exceeded ▪ The MME of each claim that contributed to the cumulative MME that exceeded the limit ▪ Total combined MME of all claims that contributed to the incoming claim exceeding the limit o Medicaid pharmacists can change values in fields of the calculator to offer suggestions to prescriber • A report was run to determine participants over 90 MME in the previous 90 days prior to the implementation date. Prior authorizations were entered into the system for those recipients for 1 year. A total of 3,669 members had PAs entered into the First Rx adjudication system. Medicaid pharmacists are performing direct case by case interventions on these participants. **Reports** ▪ Recipients on opioids Calendar Q3 2017 totaled 13,278. o Chronic utilizers with more than 90 days above the MME limit totaled 1,918 for the quarter. ▪ Statistics were presented on o Top 20 opioids prescribed o Top 20 pharmacies dispensing opioids o Top 20 members (names blacked out) with highest daily MME. ▪ Range 1,578 to 4,740 MME ▪ Update on quarterly changes in opioid utilization o 8.52% decrease in number of participants on opioids from calendar Q 1 2017 to Q 3 2017

		○ 8.35 % decrease in number of participants on opioids > 90 MME from calendar Q 1 2017 to Q 3 2017. The committee recommended the Department also pursue the plan to limit participants to a 3 to 7-day fill of opioids. It was recommended that a communication be issued to providers giving advance notice that as of a certain date this action would take place.
Public Comment Period	*Phil Petersen, MD* *Keshia Schneider*	**Public Comment Period** Marc Jensen, representing the Pfizer Medical Team, was pre-approved to provide testimony to present a double-blind, head-to-head randomized controlled trial of Xeljanz that was considered new and was not included in Provider Synergy class review information.
Drug Class Reviews and Committee Recommendations	*Sarah Martinez, PharmD* *Magellan Health Services*	**Drug Class Reviews and Committee Recommendations** Committee members were asked to base their recommendations for each drug class on the answers to the following questions: 1. Is there comparative evidence to support clinically significant differences in efficacy or effectiveness between agents? If yes, what are the differences? 2. Is there comparative evidence to support clinically significant differences in safety between agents? If yes, what are the differences? 3. Are there any agents that the committee feels strongly must be preferred or non-preferred? 4. Are there any recommendations for changes to PA requirements?
➢ *Anti-Allergens, Oral*	*Sarah Martinez, PharmD*	**Anti-Allergens, Oral** Dr. Martinez reported on **a** focused update on sublingual allergen therapy (SLIT) published by the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma, and Immunology (ACAAI). They recommended that SLIT only be used for FDA-approved indications and stated that SLIT may not be suitable for all patients (e.g., those with severe, unstable, or uncontrolled asthma, or with a history of severe systemic reaction to any form of immunotherapy). In addition, they recommended that SLIT should be used cautiously during pregnancy/breastfeeding. They emphasized that initial doses should be taken in the presence of a health care professional and that all patients should receive a prescription for self-injectable epinephrine. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents for the specific allergens by class.

➢ *Antihistamines, Minimally Sedating*	*Sarah Martinez, PharmD*	**Antihistamines, Minimally Sedating** Dr. Martinez reviewed the quarterly utilization of the drugs in this class. She reviewed the availability of three new formulations of drugs in this class: loratadine capsule OTC, Xyzal solution OTC, and Xyzal tablet OTC. She reviewed the indications and dosing of the Xyzal OTC formulations. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Immunomodulators, Atopic Dermatitis*	*Sarah Martinez, PharmD*	**Immunomodulators, Atopic Dermatitis** Dr. Martinez reported that there are two products in this class that have not been reviewed previously by this committee, Eucrisa (crisaborole) and Dupixent (dupilumab). These new agents have provided additional alternative treatment options with different mechanisms of action for atopic dermatitis. Eucrisa (crisaborole) is indicated for the topical treatment of mild to moderate atopic dermatitis in patients two years and older. Warnings include hypersensitivity reactions. Application site pain is the most common adverse effect. This agent has only been studied in two vehicle-controlled (placebo) trials. Dupixent (dupilumab) is a subcutaneous injectable indicated for the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Warnings include hypersensitivity, conjunctivitis/keratitis, and comorbid asthma. It also has no comparative evidence available, being studied only in placebo-controlled trials. It can be used with or without topical corticosteroids. Dr. Martinez reviewed the American Academy of Allergy, Asthma, and Immunology (AAAAI) 2012 guidelines which like the American Academy of Dermatology (AAD) guidelines state that pimecrolimus and tacrolimus are reasonable treatment options for patients as first-line treatment choices, in addition to hydration (emollients) and topical corticosteroids. Eucrisa and Dupixent were not available at the time of the guidelines. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy,

		effectiveness or safety between the agents. It was recommended to consider Eucrisa for preferred status as a safe alternative steroid extender agent particularly in younger children. Therapeutic criteria should include FDA approved age and diagnosis. It was recommended that Dupixent be non-preferred and prior authorized for atopic dermatitis flares with requirements of at least 2 prior treatments with topical steroids within a 6-month period.
➢ *Epinephrine, Self-Injected*	*Sarah Martinez, PharmD*	**<u>Epinephrine, Self-Injected</u>** Dr. Martinez reviewed the quarterly utilization of the available formulations. She reported that the American American Academy of Pediatrics (AAP) updated their 2007 guidance on the use of epinephrine for anaphylaxis. They recommend that at-risk patients be prescribed an epinephrine auto-injector for first line treatment of anaphylaxis, particularly if they have asthma. AAP now recommends against antihistamines for first line treatment of anaphylaxis. It was noted that the manufacturer of Auvi Q no longer offers a federal rebate to CMS so the drug is no longer payable by Medicaid. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Intranasal Rhinitis Agents*	*Sarah Martinez, PharmD*	**<u>Intranasal Rhinitis Agents</u>** There were no new agents and no recent clinically significant information in this class to report. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. They recommended that there be at least one preferred choice in each sub-class (anticholinergic, antihistamine, corticosteroid). They recommended that Dymista remain non-preferred.
➢ *Glucocorticoids, Inhaled*	*Sarah Martinez, PharmD*	**<u>Glucocorticoids, Inhaled</u>** Dr. Martinez reported that there are three new products on the market in this class: ArmonAir RespiClick (fluticasone), AirDuo RespiClick (fluticasone propionate/salmeterol), and fluticasone/salmeterol, generic for AirDuo. She reviewed the indications, dosing, contraindications, warnings, adverse effects and drug interactions for each of these agents. She also reviewed the clinical trial results for the AirDuo RespiClick. Dr. Martinez reviewed the 2017 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. They report that combination bronchodilator use may be more appropriate in patients with less advanced disease, but data does not definitively show

		LAMA/LABA (long-acting muscarinic plus long-acting beta agonist) combination treatment to be more effective than ICS/LABA (inhaled corticosteroid/long-acting beta agonist) combination treatment. Dr. Martinez reported that Symbicort is now approved for use as long-term maintenance treatment of asthma in patients 6 years of age and older (previously approved for 12 years of age and older). **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety among the agents. The committee asked that the Department when making their decision, consider the administrative burden of having to switch many patients from one agent, formerly on the PDL to another after the initial agent has been dropped from the PDL. They also asked that LABAs in the combination products which were designated preferred be the same LABA as the preferred single LABA products.
➢ *Bronchodilators, Beta Agonists, Short-Acting*	*Sarah Martinez, PharmD*	**<u>Bronchodilators, Beta Agonists, Short-Acting</u>** Dr. Martinez reported that there is one new product on the market, levalbuterol HFA which is the authorized generic for Xopenex HFA. Dr. Martinez reported that the 2017 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines relate that combination bronchodilator use may be more appropriate in patients with less advanced disease, but data does not definitively show LAMA/LABA treatment to be more effective than ICS/LABA. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Bronchodilators, Beta Agonists, Long-Acting*	*Sarah Martinez, PharmD*	**<u>Bronchodilators, Beta Agonists, Long-Acting</u>** There were no new agents to report in this class. Dr. Martinez reported that the 2017 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines relate that combination bronchodilator use may be more appropriate in patients with less advanced disease, but data does not definitively show LAMA/LABA treatment to be more effective than ICS/LABA. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy,

		effectiveness or safety between the agents.
➢ *Leukotriene Modifiers*	*Sarah Martinez, PharmD*	**Leukotriene Modifiers** Dr. Martinez reviewed the utilization data. She reported that zileuton extended release is now available as the generic equivalent for Zyflo CR. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy or effectiveness between the agents. The committee stated that there is a safety issue with zileuton and liver toxicity and it should remain non-preferred for that reason.
➢ *COPD Agents*	*Sarah Martinez, PharmD*	**COPD Agents** Dr. Martinez reviewed the utilization of the current agents in this class. She reported that the 2017 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines relate that combination bronchodilator use may be more appropriate in patients with less advanced disease, but data does not definitively show LAMA/LABA treatment to be more effective than ICS/LABA. Dr. Martinez also reported that Spiriva Respimat is now indicated for use in patients 6 years of age and older for long-term treatment of asthma (previously approved for asthma in patients 12 years of age and older, also indicated for COPD in adults). The Spiriva Handihaler is only approved for adults with COPD. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy or effectiveness as reported differences were statistical and not necessarily clinical as they related to FEV_1 values vs patient reported outcomes. They concluded that there was not any evidence of differences in safety.
➢ *Immunomodulators, Asthma*	*Sarah Martinez, PharmD*	**Immunomodulators, Asthma** There were no new agents and no recent clinically significant information in this class to report. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
Hepatitis C Utilization Update	*Mark England, PharmD* *Magellan Medicaid Administration*	**Hepatitis C Utilization Update** Dr. England presented an update of Hepatitis C utilization for the third calendar quarter of 2017. During this period, 50 requests were reviewed, with 20 approved and 19 denied. The

		remaining 11 requests were pended for requested additional information. Of the approved requests, there were 11 for Harvoni and 9 for Epclusa. The majority of approved requests were for Genotype 1 (12), with 1 approved request for Genotype 2, 5 for Genotype 3, 1 for Genotype 4, and 1 for Genotype 6. The current criteria for these agents are based on liver fibrosis staging and current approval is for F2, F3 and F4 stages. Of the approved requests, 12 were a stage of F2, 4 patients were a stage of F3 and 4 were F4. 55% of patients approved had a history of cirrhosis and 45% had no history of cirrhosis. Cirrhosis status is an important indicator for choice of treatment and duration of treatment. The majority of denials were for not meeting required liver staging criteria. Five requests were denied for active history of drug abuse. Dr. Eide is currently evaluating cost models involving Hepatitis C agents for the possibility of options to expand coverage to patients with lower fibrosis staging that meet all other criteria.
Hepatitis C – New Agents	*Sarah Martinez, PharmD*	**Hepatitis C (New Agents)** This was a review of new agents only. Dr. Martinez reported that there are two new products in this class. Mavyret (glecaprevir/pibrentasvir) is approved to treat adults with chronic HCV genotypes 1-6 without cirrhosis or with Child-Pugh A cirrhosis, including patients with moderate to severe kidney disease and those who are on dialysis. It is also approved for adults with HCV genotype 1 infection who have been previously treated with a regimen, either containing an NS5A inhibitor or an NS3/4A protease inhibitor but not both. As with other agents, there is a boxed warning for Hepatitis B Virus reactivation. It is the first agent with FDA approval for a shorter 8-week duration in the appropriate patients. Among the available treatments, it offers the shortest treatment duration to the broadest eligible patient population. She reviewed dosing, contraindications, warnings and common adverse reactions as well as clinical studies. Vosevi (sofosbuvir/velpatasvir/voxilaprevir) is indicated for the treatment of adult patients with chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have genotype 1-6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor or genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor. This is the first product FDA-approved for use in patients who have failed prior direct acting antiviral therapy. This product addresses a previous gap in care representing approximately 7.3% of HCV patients. Vosevi is not recommended in patients with moderate or severe hepatic impairment (Child-Pugh B or C). There is a boxed warning regarding hepatitis B virus

		(HBV) reactivation in patients coinfected with HCV and HBV; all patients should be tested for evidence of current or prior HBV infection before initiation of HCV treatment. Lastly, bradycardia with amiodarone coadministration may occur. She reviewed dosing, contraindications, warnings and adverse effects as well as clinical studies used for approval. **Committee Recommendations** The committee concluded that all of the agents had high efficacy above 90%, but that Mavyret offered significant advantages of being pan-genotypic with efficacy at 8 weeks of treatment. They concluded that there were not significant differences in safety as all were reasonably non-toxic. They recommended expanding treatment options to F0 when it was economically feasible to do so. They also requested that the Department consider removing the requirement for specialist consultation.
➢ *Smoking Cessation*	*Sarah Martinez, PharmD*	**<u>Smoking Cessation</u>** There were no new agents in this class to report**.** Dr. Martinez reported that the boxed warning regarding serious adverse effects on mood, behavior, and thinking has been removed from Chantix and Zyban labeling. **Committee Recommendations** The committee concluded that there is clinically significant difference in efficacy and effectiveness as mechanistically Chantix is clearly the most effective agent in this class. At the same time, there are safety issues with Chantix. After extensive discussion, the committee recommended elimination of the PA requirement for a patient's first prescription of Chantix. The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the nicotine replacement agents.
➢ *Immune Globulins*	*Sarah Martinez, PharmD*	**<u>Immune Globulins</u>** Dr. Martinez reported that there are five new products in this class: Cuvitru (subcutaneous), Hyperrab, Hyperhep B and Imogam Rabies-HT (intramuscular). The latter three agents are specialty drugs for the treatment of rabies and Hepatitis B, and for that reason were not reviewed at this time. She reviewed clinical information pertinent to Cuvitru (immune globulin, human) which is indicated for replacement therapy for primary humoral immunodeficiency in patients two years and older. This agent is contraindicated in patients with antibodies against IgA and a history of hypersensitivity. There is a boxed warning for thrombosis, and additional warnings include renal function monitoring, aseptic meningitis syndrome, hemolysis monitoring, and pulmonary adverse reactions.

		In other product updates, Dr. Martinez reported that Gamunex-C is now indicated for subcutaneous (SC) use in primary humoral immunodeficiency in pediatric patients (previously approved for SC use for this indication in adults only, among other uses). Gammaplex is now available as a 10% solution for IV administration (also available as a 5% solution) and Privigen is now approved for the treatment of adults with chronic inflammatory demyelinating polyneuropathy (CIDP) to improve neuromuscular disability. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. Dr. Brown recommended separating this class into two categories, to make a clear distinction between the disease specific agents and the general immunotherapeutic drugs in the class.
➢ *Botulinum Toxins*	*Sarah Martinez, PharmD*	**Botulinum Toxins** Dr. Martinez reported that Dysport is now indicated for the treatment of spasticity in adults. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents for like indications. The committee recommended that all agents continue to require prior authorization.
➢ *Cytokine/CAM Agents*	*Sarah Martinez, PharmD*	**Cytokine/CAM Agents** Dr. Martinez reported on five new agents in this class. • Inflectra (infliximab-dyyb) and Renflexis (infliximab-abda) are biosimilar tumor necrosis factor (TNF) blockers approved for the same indications as infliximab (Remicade), except for pediatric ulcerative colitis. • Kevzara (sarilumab) is an IL-6 receptor antagonist indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs). • Siliq (brodalumab) is indicated for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic treatment or phototherapy and have failed or no longer respond to other systemic treatments • Tremfya (guselkumab) is an interleukin-23 blocker indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. She reviewed dosing, warnings, adverse effects and distribution mechanisms for all of the new agents as well as clinical studies surrounding their approval.

		Dr. Martinez also did an update on the EXXELERATE trial comparing the efficacy of adalimumab and certolizumab with background methotrexate therapy in adult patients with rheumatoid arthritis. She also provided updates for existing products. o Ilaris is now indicated for Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS), mevalonate kinase deficiency (MKD), and familial Mediterranean fever (FMF). It was previously indicated only for cryopyrin-associated periodic syndromes (CAPS) and active systemic juvenile idiopathic arthritis. o Ilaris is also now available as a 150 mg/mL solution in single-dose vials, eliminating the need for reconstitution. The lyophilized formulation will be discontinued over time. o Stelara is now indicated for treatment of adults with moderate-to-severe Crohn's disease who have failed or were intolerant to immunomodulators or corticosteroids, but never failed or were intolerant to a TNF inhibitor (previously approved for treatment of moderate-to-severe plaque psoriasis and active psoriatic arthritis). o Enbrel is now indicated for the treatment of plaque psoriasis in patients four to 17 years old (previously indicated only for adults with this indication). o Actemra is now approved for giant cell arthritis (GCA) in adults. o Actemra intravenous injection is now approved for patients 2 years of age or older with chimeric antigen receptor (CAR)-T cell-induced severe or life-threatening cytokine release syndrome (CRS). o Enbrel Mini, a 50 mg/mL single-dose, pre-filled cartridge for use with the AutoTouch reusable autoinjector has been FDA-approved. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents for specific indicated uses. It was recommended to make sure there was at least one preferred agent available for each common indication. It was also proposed that this class be subdivided into two groups, TNF inhibitors and non-TNF agents on the PDL Document. There was a recommendation to have Enbrel preferred if cost effective at least for age less than 13 years.
➢ *Ophthalmic Antibiotics*	*Sarah Martinez, PharmD*	**<u>Ophthalmic Antibiotics</u>** Dr. Martinez reported that Vigamox safety and efficacy has now been established in all

		pediatric ages and that it is now available generically. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Ophthalmic Antibiotic/Steroid Combinations*	*Sarah Martinez, PharmD*	**<u>Ophthalmic Antibiotic/Steroid Combinations</u>** There were no new agents and no recent clinically significant information to review in this class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. For safety concerns the committee recommended moving all neomycin agents to non-preferred status. The committee still supported prescribing of the agents in this class by an ophthalmologist whenever possible and to continue the current limit in the system for a maximum of one prescription per 60 days.
➢ *Ophthalmics, Anti-inflammatory/ Immunomodulators*	*Sarah Martinez, PharmD*	**<u>Ophthalmics, Anti-inflammatory/Immunomodulators</u>** Dr. Martinez reported that Restasis is now available as a multi-dose, preservative free preparation. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Ophthalmics for Allergic Conjunctivitis*	*Sarah Martinez, PharmD*	**<u>Opthalmics for Allergic Conjunctivitis</u>** Dr. Martinez reported that Pataday is now available as generic olapatadine. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
Other Committee Business	*Tami Eide, PharmD*	**<u>Other Committee Business</u>** There was no other committee business to discuss. Keshia will be sending an email to all members with the 2018 meeting dates, for calendaring purposes. The meeting adjourned at 2:11 p.m.

Pharmacy and Therapeutics Committee Meeting
Public Comment

Marc Jensen, Pfizer

So, good morning, my name is Marc Jensen. I am a licensed pharmacist on the Medical Affairs Team at Pfizer and I'm here today to discuss some new data—a head-to-head study of Xeljanz or tofacitinib compared to adalimumab or Humira. I'm going to spare you the long-winded education and a lot of the adverse events, which I probably should tell you, but I will refer you to the package insert that's on the website for that information. I will let you know that Xeljanz or tofacitinib is indicated for adults with moderate to severe rheumatoid arthritis with some other caveats as well. So, I'd like to quickly review the latest Phase 3 tofacitinib member Xeljanz study published just this July in the journal *Lancet*. It was called 'The Oral Strategy' and it was a Phase 3b/4, 12-month, double-blind, head-to-head, non-inferiority, randomized, controlled trial conducted to assess the comparative efficacy and safety of tofacitinib monotherapy versus combination tofacitinib with methotrexate and the adalimumab combination with methotrexate.

None of the prior six Phase 3 tofacitinib trials had evaluated tofacitinib monotherapy versus tofacitinib combination therapy. The study enrolled over 11,000 patients and they were randomized equally to one of the following treatment arms: tofacitinib 5 mg OD monotherapy, tofacitinib 5 mg OD in combination with methotrexate, or adalimumab 40mg in combination with methotrexate. The primary endpoint was an improvement in signs and symptoms, defined as a 50% improvement in American College of Rheumatology score, or the ACR50, at 6 months. A number of other secondary endpoints, including achievement of low disease activity and remission, were also included and assessed in the study. At 6 months, that ACR50 response was attained in 38% of patients who received tofacitinib monotherapy, 46% of patients who received tofacitinib plus methotrexate, and 44% of patients who received the adalimumab plus methotrexate combination. Tofacitinib methotrexate was deemed non-inferior to adalimumab plus methotrexate. Non-inferiority was not demonstrated for tofacitinib monotherapy versus either combination arm. The proportion of patients who achieved low disease activity and remission were similar between the combination arms, which were higher numerically than in the tofacitinib monotherapy arm.

In this 12-month study, the authors noted no new unexpected safety issues in any treatment arm. Most adverse events were mild or moderate in nature, and the most common adverse events were upper respiratory tract infection, LFT elevation, nasopharyngitis, UTIs and nausea. Changes in laboratory parameters were noted in each treatment group. The incidence of liver function test elevations were higher in either combination group compared to tofacitinib monotherapy. The authors concluded that similar safety and efficacy were noted with tofacitinib plus methotrexate and adalimumab with methotrexate.

So, in conclusion, this is the seventh phase 3 randomized, controlled trial of tofacitinib RA, part of a program evaluating the safety and efficacy of

tofacitinib in a wide range of RA patients. The oral medication has been studied in over 6,300 patients with over 21,000 patient years of drug exposure. Xeljanz is a useful option in combination with other non-biologic DMARDs or as monotherapy to have available on the PDL as a preferred agent for those patients who cannot tolerate methotrexate or have not adequately responded to methotrexate or biologic-based therapies, due to its unique mechanism of action, established safety and efficacy, and availability as an oral dosage form. Thanks for your time and I'll take any questions you might have about the study.

Alright, thank you very much.