References on the Administration of Statin Class Drugs Using ALZET® Osmotic Pumps

**Atorvastatin**


**Agents:** Atorvastatin  
**Vehicle:** CSF, artificial;  
**Route:** CSF/CNS;  
**Species:** Mice;  
**Pump:** Not Stated;  
**Duration:** 3 weeks;

**ALZET Comments:** Dose (1 ug or 5 ug); animal info (Male, C57BL/6, 25-30 g, 2 months old); behavioral testing (Open Field Test, Tail Suspension Test, Sucrose Preference Test, Novelty Suppressed Feeding Test); Brain coordinates ((− 0.7 mm posterior to the bregma; ± 1.2 mm lateral to the sagittal; 2.0 mm below dura); bilateral cannula used; immunology;


**Agents:** Punicalagin, Quercetin, Atorvastatin  
**Vehicle:** water, distilled, Tween 80;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1004;  
**Duration:** 28 days;

**ALZET Comments:** Dose (punicalagin 140μg/100 μl, quercetin 42μg/100 μl, atorvastatin 15mg/100 μl); 2% Tween 80 used; Controls received mp w/ vehicle; animal info (male Balb/c mice, 8 weeks old); no stress: Mouse BW was not affected by sc-implanted pump treatments. (see pg. 3);


**Agents:** Atorvastatin calcium  
**Vehicle:** Route: SC;  
**Species:** Mice;  
**Pump:** 2004;  
**Duration:** 12 weeks;

**ALZET Comments:** Dose (10 mg/kg/day); Controls received mp w/ vehicle; animal info (Male C57BL/6 mice (8 wk old, 18±22 g)); cardiovascular; diabetes; Therapeutic indication (diabetic cardiomyopathy);


**Agents:** Atorvastatin Vehicle: DMSO; CSF, artificial;  
**Route:** CSF/CNS;  
**Species:** Rat;  
**Pump:** 1003D;  
**Duration:** 14 days;

**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, SHRSP/Izm, WKY, 14-16 wksold)

**Fluvastatin**


**Agents:** Fluvastatin  
**Vehicle:** DMSO, Ringer's Solution;  
**Route:** Ear (cochlea);  
**Species:** Guinea Pig;  
**Pump:** 2004;  
**Duration:** 28 days;

**ALZET Comments:** Dose (fluvastatin 50 μM); animal info (Outbred Hartley guinea pigs of both sexes 200–500 g); post op. care (Buprenex); Cannula used;


**Agents:** Mevalonate; Fluvastatin  
**Vehicle:** Saline, physiological;  
**Route:** IP;  
**Species:** Pump:  
**Duration:** 5 days;

**ALZET Comments:** tissue perfusion (lesion site-carotid collar); enzyme inhibitor (HMG-CoA reductase)


**Agents:** Mevalonate; Fluvastatin  
**Vehicle:** Route: IP;  
**Species:** rabbit

**ALZET Comments:** controls received mp w/ saline; tissue perfusion (carotid artery collar); cardiovascular; enzyme inhibitor (HMG-CoA reductase)
Lovastatin
**Agents:** Phenytoin; lovastatin  **Vehicle:** Water; propylene glycol; ethanol;  **Route:** SC;  **Species:** Mice;  **Pump:** 2002;  **Duration:** 12 weeks;
**ALZET Comments:** Controls received mp w/ vehicle or saline; animal info (male, BALB/cByJ, 8 weeks old); 9% ethanol used; 41% propylene glycol used; long-term study; phenytoin and lovastatin inside one pump; used autoclips; pumps primed in 37C saline overnight;

**Agents:** Lovastatin; Pravastatin; Liposomes; Simvastatin  **Vehicle:** Propylene glycol;  **Route:** Species: Rat;  **Pump:** 2ML4;
**Duration:** no duration posted;
**ALZET Comments:** comparison of injections and oral administration vs. mp; stress/adverse reaction: local cystic reaction to simvastatin and lovastatin (p. 271, 275); enzyme inhibitor (HMG-CoA reductase), sc injections of simvastatin also caused subcutaneous toxicity

Pravastatin
**Agents:** Pravastatin;  **Vehicle:** DMSO;  **Route:** SC;  **Species:** Mice;  **Pump:** 1002;  **Duration:** 2 weeks;
**ALZET Comments:** Animal info (female, C57BL6); enzyme inhibitor (ROCK, Rho-associated protein kinase); 10% DMSO used

**Agents:** Rifampin; pravastatin  **Vehicle:** Water; DMSO;  **Route:** SC;  **Species:** Mice;  **Pump:** 2001D;
**Duration:** 24 hours;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, DBA1/lacJ, wt, Slco1b2 -/-, 9-14 wks old); 0.5% DMSO used

**Agents:** Lovastatin; Pravastatin; Liposomes; Simvastatin  **Vehicle:** Propylene glycol;  **Route:** Species: Rat;  **Pump:** 2ML4;
**Duration:** no duration posted;
**ALZET Comments:** comparison of injections and oral administration vs. mp; stress/adverse reaction: local cystic reaction to simvastatin and lovastatin (p. 271, 275); enzyme inhibitor (HMG-CoA reductase), sc injections of simvastatin also caused subcutaneous toxicity

Rosuvastatin
**Agents:** Rosuvastatin, Angiotensin II  **Vehicle:** Saline;  **Route:** SC;  **Species:** Mice;  **Pump:** 2004;  **Duration:** 5 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (apoE -/-, 8 weeks old); cardiovascular; peptides; “Because the s.c. administration of the statin using an osmotic minipump allows 100% drug bioavailability and its p.o. administration results in 34.5% bioavailability in mice (Peng et al., 2009), we chose the former route to ensure a full dosage effect.” pg 2948;

Q3875: P. Escudero, et al. Combined Sub-Optimal Doses of Rosuvastatin and Bexarotene Impair Angiotensin II-Induced Arterial Mononuclear Cell Adhesion Through Inhibition of Nox5 Signaling Pathways and Increased RXR/PPARalpha and RXR/PPARgamma Interactions. ANTIOXIDANTS & REDOX SIGNALING 2015;22(901-920
**Agents:** Angiotensin II; Rosuvastatin  **Vehicle:** Saline;  **Route:** SC;  **Species:** Mice;  **Pump:** Duration: 14 days;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL6 or ApoE -/-, 23-30g); cardiovascular; peptides; antihypertensive;

**Agents:** Rosuvastatin  
**Vehicle:** NaCl;  
**Route:** CSF/CNS;  
**Species:** Mice;  
**Pump:** 2004;  
**Duration:** 4 weeks;  
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (C57BL6/J, 23-25 g); ALZET brain infusion kit 3 used; enzyme inhibitor (HMG-CoA reductase)

**Simvastatin**


**Agents:** Simvastatin  
**Vehicle:** DMSO/PEG;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 2002;  
**Duration:** 14 days;  
**ALZET Comments:** Dose (20 mg/kg/day); Controls received mp w/ vehicle; animal info (14 weeks old, Male, C57BL/6, Parkin KO); behavioral testing (Open Field Test); dependence;


**Agents:** Simvastatin  
**Vehicle:** PBS;  
**Route:** SC;  
**Species:** Mice (nude);  
**Pump:** 2006;  
**Duration:** ALZET Comments: Dose (11 mg/kg/day); 40% DMSO, 60% PBS used; Controls received mp w/ vehicle; animal info (6 week old male Athymic Nude-Foxn1Nu mice);


**Agents:** Simvastatin  
**Vehicle:** Polyethylene glycol;  
**Route:** SC;  
**Species:** Rat;  
**Pump:**  
**Duration:** ALZET Comments: Control animals received mp w/ vehicle; animal info (9 wks old, male, Wistar)

Q0763: P. Wei, et al. Simvastatin Reverses Podocyte Injury but not Mesangial Expansion in Early Stage Type 2 Diabetes Mellitus. RENAL FAILURE 2009;31(6):503-513

**Agents:** Simvastatin  
**Vehicle:** Ethanol;  
**Route:** SC;  
**Species:** Mice;  
**Pump:**  
**Duration:** 4 weeks;  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (C57BL/6, male, 26 wks old); 60% ethanol used


**Agents:** Simvastatin  
**Vehicle:** Route: CSF/CNS;  
**Species:** Rat;  
**Pump:** 2004;  
**Duration:** 4 weeks;  
**ALZET Comments:** Comparison of PO gavage vs. mp; ALZET brain infusion kit used; post op. care (buprenorphine); animal info (female, Long Evans, adult, 200-22 g.); cannula placement confirmed by preparing cryosections of the brain at the lateral ventricle and verifying the presence of a cavity created by the cannula; spinal cord injury


**Agents:** Simvastatin  
**Vehicle:** PEG 400;  
**Route:** SC;  
**Species:** Mice;  
**Pump:** 1002;  
**Duration:** 14 days;  
**ALZET Comments:** Comparison of SC injections vs. SC mp vs. localized delivery; half-life (p. 2 of 6) “about 2 hours in humans”; animal info (mature, male, Balb-C); tissue perfusion (femur); compound passed through sterile filter before filling in pumps; silicone tube used; “continuous systemic delivery resulted in a 160% larger force at failure.”; “Continuous local delivery... resulted in a 170% larger force at failure as well as a twofold larger energy uptake.”


**Agents:** Simvastatin  
**Vehicle:** Water, distilled;  
**Route:** SC;  
**Species:** Rat;  
**Pump:**  
**Duration:** ALZET Comments: Controls received no treatment; animal info (male, Sprague-Dawley, 225-250 g)
**Agents:** Lovastatin; Pravastatin; Liposomes; Simvastatin  
**Vehicle:** Propylene glycol;  
**Route:** Species: Rat;  
**Pump:** 2ML4  
**ALZET Comments:** comparison of injections and oral administration vs. mp; stress/adverse reaction: local cystic reaction to simvastatin and lovastatin (p. 271, 275); enzyme inhibitor (HMG-CoA reductase), sc injections of simvastatin also caused subcutaneous toxicity

**Pitavastatin**


**Agents:** Pitavastatin; Wortmannin; Y-27632 
**Vehicle:** DMSO; saline;  
**Route:** SC;  
**Species:** Rat;  
**Pump:** 2ML4;  
**Duration:** 7 weeks;  
**ALZET Comments:** Controls received mp w/ vehicle; long-term study; pumps replaced; enzyme inhibitor (phosphatidyl inositol 3-kinase, Rho kinase); cardiovascular; multiple pumps per animal (2); animal info (male, Dahl S, Dahl R, 11 wks old); 8% DMSO used