comparative bioavailability of one dose of INFS with transmucosally administered Actiq were assessed.
Methods: In a randomised, single-center, open-label, 2-way crossover pharmacokinetic study 24 subjects (12 male, 12 female, mean age of 25.2 years, mean BMI 24.6 kg/m^2) received INFS 200 μg/100 μL and Actiq (buccal lozenge, 200 μg). Naltrexone was given to prevent potential adverse reactions. Frequent plasma samples were taken up to 96 hours and analysed by LC-MS/MS with a lower limit of quantitation of 25 pg/mL. Primary pharmacokinetic parameter was the area under the fentanyl plasma concentration-time curve (AUC(0-∞)).
Results: Compared to Actiq, a much faster absorption rate was observed for INFS, which is supported by the much earlier appearance of detectable fentanyl plasma levels and a shorter T_{max}. At 15-minutes postdose, the mean plasma fentanyl levels reached 602 pg/mL and 29 pg/mL for intranasal fentanyl and Actiq, respectively. Significantly higher C_{max} and AUC values were obtained with INFS compared to Actiq. Although administered for 15 minutes according to the approved US product labeling, consumption of Actiq was incomplete in many incidences (70%) upon visual inspection. No safety concerns were identified with INFS administration in combination with oral naltrexone.
Conclusions: One dose of fentanyl nasal spray is significantly more bioavailable than Actiq based on dose-normalized AUC.
This study was sponsored by Nycomed.

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PHARMACOKINETICS OF INTRANASAL FENTANYL SPRAY (INFS) IN SUBJECTS WITH SEASONAL ALLERGIC RHINITIS WITH AND WITHOUT PRIOR ADMINISTRATION OF OXYMETAZOLINE

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Background and Aims: Intranasal fentanyl spray (INFS) was developed for the treatment of breakthrough pain in cancer patients using a new route of administration. The potential effect of prior administration of the vasoconstrictor oxymetazoline on the rapid absorption of INFS in subjects with seasonal allergic rhinitis (SAR) was assessed.
Methods: In a randomised, single-center, open-label, 2-way crossover pharmacokinetic study 12 subjects (8 male, 4 female, mean age of 23.8 years, mean BMI 23.8 kg/m^2) with SAR received INFS 200 μg/100 μL with and without oxymetazoline spray (1 hour prior to INFS dosing). Naltrexone was given to prevent potential adverse reactions. Frequent plasma samples were taken up to 72 hours and analysed by LC-MS/MS with a lower limit of quantitation of 25 pg/mL. The primary pharmacokinetic parameter was the area under the plasma concentration time curve (AUC(0-∞)).
Results: Following administration of INFS the prior treatment with oxymetazoline significantly decreased peak fentanyl plasma concentration and prolonged the absorption time of fentanyl. However, comparable AUC(0-∞) results were achieved between both treatments as shown by the ratio of estimated geometric means of 1.01 (90% confidence interval: 0.71–1.44). No safety concerns were identified for INFS, with or without oxymetazoline, administered in combination with oral naltrexone.
Conclusions: Despite differences in the maximum plasma concentration (C_{max}) and time to maximum plasma concentration (T_{max}), the extent of fentanyl exposure (AUC(0-∞)) in allergic rhinitis subjects after prior treatment with a nasal constrictor is comparable to that in subjects without prior treatment.
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PHARMACOKINETICS OF INTRANASAL FENTANYL SPRAY (INFS) IN SUBJECTS WITH COMMON COLD

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Background and Aims: Intranasal fentanyl spray (INFS) was developed for the treatment of breakthrough pain in cancer patients using a new route of administration. The primary objective was to assess whether upper respiratory infections in the form of the common cold alter the absorption of INFS in subjects.
Methods: In a single-center, open-label pharmacokinetic (PK) study 8 subjects (4 male, 4 female, mean age of 29.8 years, mean BMI 23.1 kg/m^2) with common cold received INFS 200 μg/100 μL. Naltrexone was given to prevent potential adverse reactions. Frequent plasma samples were taken up to 48 hours and analysed by LC-MS/MS with a lower limit of quantitation of 25 pg/mL. The primary PK parameter was the area under the plasma concentration time curve (AUC(0-∞)). The PK results were compared to those of 8 healthy subjects closely matched for gender, BMI, and age who received the same dose in other INFS PK studies.
Results: The systemic exposure of fentanyl is similar to what has been observed in healthy subjects as demonstrated by comparable AUC results. Following INFS the $AUC_{(0-\infty)}$ was 4164±1102 pg·h/mL for subjects with a common cold and 4015±1406 pg·h/mL for matched healthy subjects, respectively. No safety concerns were identified with INFS administered in combination with oral naltrexone.
Conclusions: Following administration of intranasal fentanyl, an upper respiratory infection does not alter the absorption of fentanyl suggesting no need for dose adjustment in patients with a common cold.
This study was sponsored by Nycomed.

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PHARMACOKINETICS AFTER ADMINISTRATION OF 100 μG INTRANASAL FENTANYL SPRAY (1 DOSE VS. 2 DOSES) IN NON-ELDERLY AND ELDERLY HEALTHY SUBJECTS

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Background and Aims: Intranasal fentanyl spray (INFS) was developed in different dose strengths for the treatment of breakthrough pain in cancer patients. Pharmacokinetic parameters following two dosing regimens were assessed in non-elderly and elderly healthy subjects.
Methods: In a randomised, single-center, open-label, 2-way crossover study, 16 non-elderly (mean age 27.7 years) and 7 elderly subjects (mean age 73.6 years) received 100 μg fentanyl delivered as 1 dose of INFS 100 μg/100 μL or 2 doses of INFS 50 μg/100 μL (1 dose in each nostril) using a multi-dose device. Naltrexone was given to prevent potential adverse reactions. Frequent plasma samples were taken up to 72 hours and analysed by LC-MS/MS (lower limit of quantitation: 25 pg/mL). Primary pharmacokinetic parameters were AUC(0-∞) and C_{max}.
Results: Non-elderly and elderly healthy subjects showed similar pharmacokinetic profiles for both dosing regimens. Mean fentanyl C_{max} and AUC values in all subjects following the administration of 1 dose of 100 μg/100 μL were 449 pg/ml and 2080 pg·h/mL, respectively. For the other regimen, corresponding mean C_{max} and AUC values were 339 pg/ml and 1779 pg·h/mL. No safety concerns were identified with INFS administered in combination with oral naltrexone.
Conclusions: A moderately lower rate and extent of fentanyl exposure (C_{max} and AUC) were observed following the administration of 2 doses of 50 μg/100 μL compared with that after