SUMMARY OF FINAL REPORT OF OBSERVATIONAL, INTERNATIONAL, MULTICENTER NON-INTERVENTIONAL CLINICAL STUDY QLIFE

Study Title:

Impact of naproxen sodium (Nalgesin® forte) treatment on the performance of daily activities in patients with low back pain or osteoarthritis in regular clinical practice

The main aim of this study was to gather and analyse therapeutic data on the effectiveness of Krka's naproxen sodium in reducing pain and improving the ability to perform activities of daily living (such as mobility, daily routines, social interactions, and general well-being) in patients with low back pain (LBP) or osteoarthritis (OA) in routine clinical settings. In addition, the study aimed to assess the frequency of adverse events associated with treatment using Krka's naproxen sodium throughout the study period. Furthermore, it aimed to evaluate the overall impact of this treatment on improving patient well-being and daily activities in real-world clinical practice.

The study hypothesized that the use of Krka's naproxen sodium would effectively reduce pain and enhance the quality of daily functioning in patients with LBP or OA.

In total 2767 patients (89.8%) reported improved **mobility**, 2708 patients (87.9%) experienced improved in **daily routine**, **socialization** improved in 2402 patients (78.0%) and general **well-being/mood swing** improved in 2641 patients (85.7%).

Patients were observed over the course of 4 weeks and investigators were required to record data at two time points. The first data collection (1st data capture) was at patient's inclusion in the study and the second data collection (2nd data capture) was up to 4 weeks from patients' inclusion in the study. Patient's visits were performed in line with regular clinical practice in each participating country. These countries are Bosnia and Hercegovina, Kazakhstan, Mongolia, North Macedonia, Slovenia, and Serbia. At the end of observation more than **92.4% of patients were very satisfied or satisfied** with the treatment with Krka's naproxen sodium.

Selection of investigators

All together **198** investigators participated in this study. Among all of them, **59.1%** were **GPs** (N=117), 9.1% neurologists (N=18), 7.6% rheumatologists (N=15), 4.5% orthopaedists (N=9) and 19.7% other specialists (N=39).

Data collection

Out of 3081 patients 38.7% (n=1193) were male and 61.3% (n=1888) female patients. Average age of patients was 53.8 years ± 14.5 years. The oldest patient was 92 years old and the youngest 18 years old. For one patient there was no collected data about years. Patients were divided into 5 groups according to their age. 3.1% (n=95) of patients were born between 1928 and 1945 and were part of silent generation. 36.1% (n=1111) were baby boomers (born between 1946 and 1964), 35.9% (n=1107) of patients were born in the years 1965-1980 (generation X), 20.9% (n=644) were generation Y (year of birth between 1981 and 1996) and 4.0% (n=123) of patients belong to generation Z (born between 1997 and 2006).

Pain intensity

Patients' mean of current pain intensity on NRS was for all participating patients at **1st data capture** (n=3081) **5.7 ± 1.8**, the mean value of average pain intensity in the last 24 hours **5.7 ± 1.7** and the mean value of worst pain intensity in the last 24 hours was **6.4 ± 1.8**.

At **2nd data capture** mean value of patients' current pain intensity on NRS was for all participating patients (n=3081) **2.0 ± 1.5**. Mean value of average pain intensity in the last 24 hours was **2.1 ± 1.5** and mean value of worst pain intensity in the last 24 hours was **2.5 ± 1.7**. For all three pain intensities the minimum recorded value was 0 and the maximum recorded value was 9 for current pain intensity and average pain intensity in the last 24 hours and 10 for worst pain intensity in the last 24 hours.

When comparing pain intensities between both data captures, **statistically significant decreases (p<0.001) were observed for all of them**.

Table 1 and Figure 1 present changes in pain intensity for patients with data for both data captures.

Table 1: Changes in pain intensity for patients with data for both data captures.

Type of pain intensity on NRS scale	N	Mean values				95%-CI for mean absolute difference	p-value
		1st and 2nd data capture		Abs. difference	Rel. difference		
Current pain intensity	3081	5.73	2.03	-3.69	-63%	[-3.76,-3.62]	<0.001
Average PI in the last 24 hours	3081	5.71	2.07	-3.63	-62%	[-3.7,-3.56]	<0.001

Worst PI in the last 24 hours	3081	6.42	2.51	-3.91	-60%	[-3.98,-3.83]	<0.001

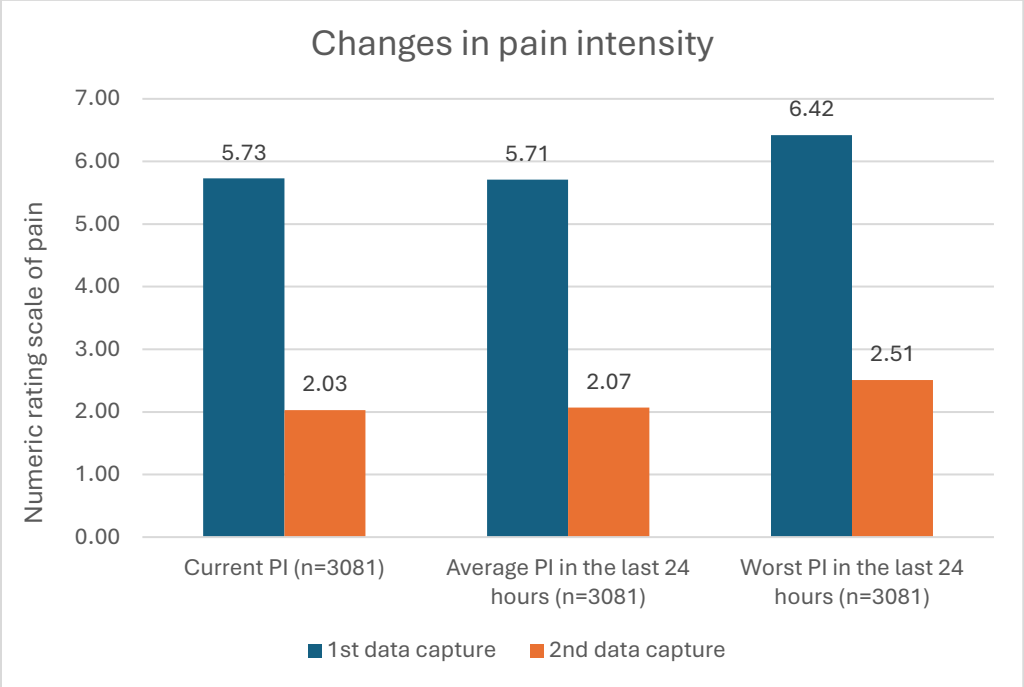

Figure 1: Changes in different pain intensities from 1st to 2nd data capture.

Mean value of average pain intensity in the last 24h on NRS for patients with compliance less than 50% (n=36) decreased from **5.67** to **3.39** (abs. difference –2.28 (95%-CI [-2.85,-1.7], rel. difference –39%). Average pain intensity in the last 24 hours also decreased in subgroup of patients with compliance 50%-80%. It went from **5.44** at 1st data capture to **2.45** at 2nd data capture (abs. difference –3.00 (95%-CI [-3.12,-2.87], rel. difference –54%). Biggest difference in average pain intensity in the last 24 hours was seen with patients whose compliance with Krka's naproxen sodium was more than 80%. Mean value decreased from **5.80** to **1.95** (abs. difference –3.85 (95%-CI [-3.93,-3.76], rel. difference –65%). Decreases in all three subgroups were **statistically significant (p<0.001)**.

At 1st data capture, investigators prescribed different dosing regimens of Krka's naproxen sodium 550 mg to patients. To most patients (n=2817; **91.4%)** investigators have prescribed **2 doses per day**. 237 patients (7.7%) were prescribed to once daily regimen and 27 patients (0.9%) to triple daily regimen.

General practitioners most often prescribed 2 doses per day (n=1471; 91.1%), followed by regimen of 1 dose per day (n=130; 8.1%). Krka's naproxen sodium 550 mg triple a day was prescribed to 13 (0.8%) patients. **Neurologists** also prescribed most common regimen of 2 doses per day (n=278; 93.3%), one daily was prescribed to 8 (2.7%) patients and three doses per day to 12 (4.0%) patients. **Orthopedists** prescribed only 2 doses per

day to 166 patients (100%). Out of all patients that were treated by **rheumatologists**, 80.0% of them received 2 doses per day (n=339) and 20% of them were treated with once per day regimen (n=85). Investigators by **other specialties** treated 579 patients, from which 97.2% (n=563) were prescribed 2 doses per day, 2.4% received Krka's naproxen sodium 550 mg once per day and less than 1% of patients received 3 doses per day (n=2; 0.3%).

Prescribed regimen by investigator's speciality was evaluated also at 2nd data capture, where in total 1320 patients prolonged the treatment with Krka's naproxen sodium 550 mg. Among all specialities single dose regimen was prescribe for 48.3% and twice daily regimen to 51.5% of patients. **General practitioners** prescribed 1 dose per day to 322 patients (47.8%), 2 doses per day to 350 (52.0%) patients and 3 doses per day to 1 (0.1%) patient. More than half of the patients (n=93; 56.4%) that were treated by **neurologists**, were prescribed twice per day regimen and 43.6% (n=72) of them were prescribed 1 dose per day. **Orthopedists** have prescribed 1 dose per day to 19 (16.8%) patients, more than 80% (n=93; 82.3%) were still receiving 2 does per day and 1 patient received 3 doses per day (0.9%). **Rheumatologists** most prescribed 1 dose of Krka's naproxen sodium 550mg at 2nd data capture (n=89; 67.4%) and to little more than 32% of patients were prescribed 2 doses per day (n=43; 32.6%). **Other investigators** specialities prescribed 1 dose to 135 patients (57%), 2 doses per day to 101 patients (42.6%) and 3 doses per day to one patient (0.4%).

Out of 3081 patients at 2nd data capture, **57.2%** stated that it is **very important** to them to take prescribed pain reliever two times per day instead of three times per day or more. Approximately 38% of patients (n=1181; **38.3%)** indicated that 2-times-daily dosing regimen is **important** to them and to 4.4% of patients (n=137) it is **not important** to take prescribed pain reliever two times a day instead of three times per day or more.

Results

There were 1106 patients (35.9% of all patients with reported information about improved overall activities of daily living) whose treatment duration with Krka's naproxen sodium 550mg was not exceeding 14 days. Among them 966 (87.3%) patients reported improved abilities to perform general activities of daily living.

With treatment duration not exceeding 14 days in total 2767 patients (89.8%) reported improved **mobility**, 2708 patients (87.9%) experienced improved in **daily routine**, **socialization** improved in 2402 patients (78.0%) and general **well-being/mood swing** improved in 2641 patients (85.7%).

After an up to 4-week treatment with Krka's naproxen sodium 550mg **91.6%** (n=2822) patients reported about **improved ability to perform overall activities of daily living**.

Among women the improved ability to perform overall activities of daily living was confirmed in 91.6 % (n=1887) and among men in 91.5% (n=1193).

Table 2: Patients with improved ability to perform overall activities of daily living based on different age subgroups.

Generation	Nu. of patients with data	Nu. of patients with improved ability to perform overall activities	% of patients with improved ability to perform overall activities	95%-CI
Silent generation	95	87	91.6%	[84.1%,96.3%]
Baby boomers	1111	1008	90.7%	[88.9%,92.4%]
Generation X	1106	1024	92.5%	[90.9%,94.1%]
Generation Y	644	590	91.6%	[89.2%,93.6%]
Generation Z	123	112	91.1%	[84.6%,95.5%]

By improving the ability to perform daily activities, the positive effects of treatment with Krka's naproxen sodium 550mg were reflected in mobility, daily routines, socialization, and overall well-being/mood swings. In total 2767 patients (89.8%) reported improved **mobility**, 2708 patients (87.9%) experienced improvement in **daily routine**, **socialization** improved in 2402 patients (78.0%) and general **well-being/mood swing** improved in 2641 patients (85.7%).

In **silent generation**, 86 out of 95 patients (90.5%) reported improved mobility, 89.5% (n=85) of them got theirs daily routine advanced, 76.8% (n=73) were more socialized and general well-being/mood swings were better in 70 patients (73.7%). **Baby boomers** (n=1111) also reported about improvements with mobility (n=982, 88.4%), daily routine (n=960; 86.4%), socializing (n=849; 76.4%) and general well-being/mood swings (n=951; 85.6%). Among all generations, the biggest improvements in general were reported in **generation X** (n=1107). 91.5% (n=1013) of their patients reported about improved mobility, almost 89.8% of them (n=994) improved their daily routine, 80.2% (n=888) were better with socializing and general well-being/mood swings was improved in 958 patients (86.5%). Improvements were also seen in **generation Y** (n=644), where mobility was improved in 578 (89.8%) patients, daily routine in 561 (87.1%) patients, socializing in 505 (78.4%) patients and general well-being/mood swings were improved in 563 (87.4%) patients. Majority of the youngest generation of patients (**generation Z**) also confirmed improvements in ability to perform overall activities: mobility and daily routine were better with 87.0% of patients (n=107), socializing with 86 (69.9%) patients and general well-being/mood swings with 98 (79.7%) patients from generation Z. Figure 2 shows the distribution of patients by different improved daily activities separately by age group, with the number of total patients in each age group.

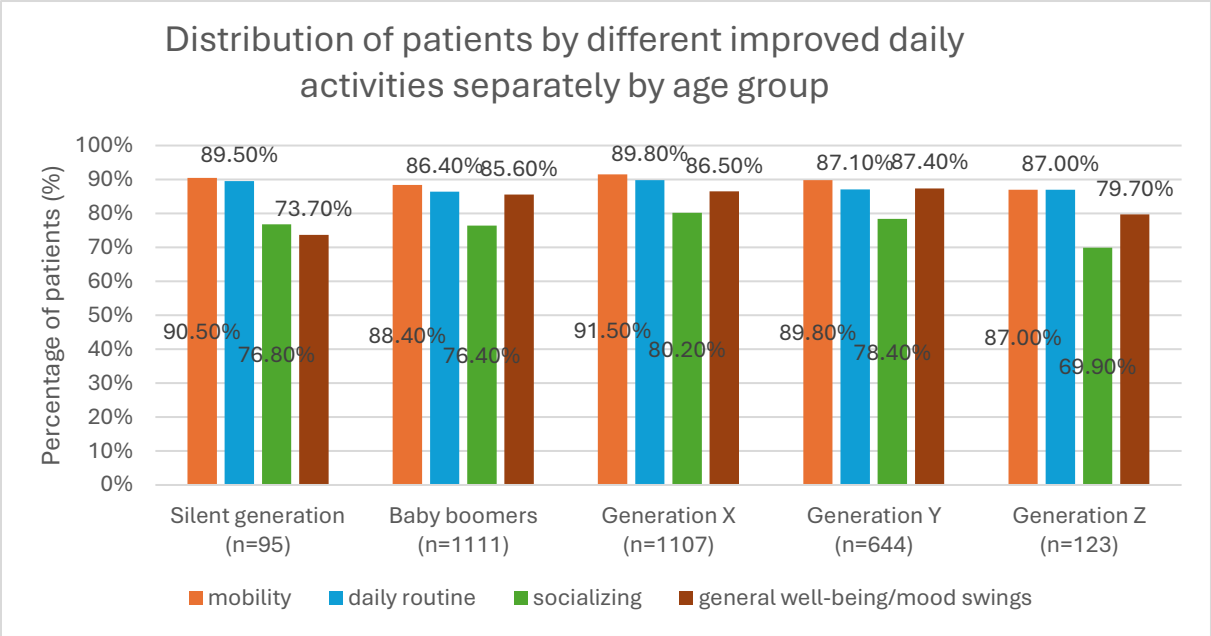

Figure 2: Distribution of patients by different improved daily activities separately by age group.

Mean absolute and relative changes in scores measuring the impact of LBP or OA on the ability to perform activities of daily living in total and in partial scores from the beginning to the end of an up to 4-week treatment with Krka's naproxen sodium are presented in Table 3. **The decreases in all scores were statistically significant** (p<0.001).

Table 3: Mean absolute and relative changes in scores measuring the impact of LBP or OA on the ability to perform activities of daily living.

Pain impact scores	Nu. of patients with data	Mean values				95%-CI for mean absolute difference	p-value
		Scores at 1st and 2nd data capture		Abs. difference	Rel. difference		
Mobility	3081	14	8.16	-5.84	-39%	[-5.99,-5.69]	<0.001
Daily routine	3081	12.38	7.16	-5.21	-40%	[-5.36,-5.06]	<0.001
Socializing	3080	5.77	3.43	-2.33	-36%	[-2.41,-2.26]	<0.001
General well-being and mood swings	3080	8.5	5.06	-3.44	-37%	[-3.54,-3.33]	<0.001
OVERALL	3080	40.65	23.82	-16.83	-40%	[-17.27,-16.39]	<0.001

Improved ability to perform overall activities of daily living was evaluated also in **different patient's subgroups based on their pain intensity**. Out of 291 patients with average pain intensity in the last 24 hours equal to 3 on NRS scale, 89.7% of them had their ability to perform overall activities improved (n=261). Among 1749 patients with

average pain intensity in the last 24 hours from 4 to 6 on NRS scale the improved ability was reported in 92.2% of them (n=1614). Among 1040 patients with average pain intensity in the last 24h hours from 7 to 10 on NRS scale, the improved ability was reported in 91.1% (n=947).

Table 4: Patients with improved ability to perform overall activities of daily living based on their pain intensity.

Division of patients based on pain intensity	Nu. of patients with data	Nu. of patients with improved ability to perform overall activities	% of patients with improved ability to perform overall activities	95%-CI
24h API equal to 3	291	261	89.7%	[85.6%,92.9%]
24h API 4 to 6	1749	1614	92.2%	[90.9%,93.5%]
24h API 7 to 10	1040	947	91.1%	[89.2%,92.7%]

Among all 3410 patients, which were included in Safety Analysis Set, 1936 were on gastroprotective medications and 1474 patients were not on gastroprotective medications.

Among patients on gastroprotective medication **only 6 patients (0.2% of all patients in SAS; 0.3% of patients on gastroprotective medication)** experienced gastrointestinal adverse events. As gastrointestinal adverse events were counted dyspepsia, epigastric discomfort, diarrhoea, abdominal pain, abdominal distension, flatulence, nausea.

These 6 patients with gastrointestinal adverse events represent 27.3% of all patients with gastrointestinal adverse events in the study and 31.6% of all patients with gastrointestinal adverse reactions in the study.

Among patients without gastroprotection **16 patients** experienced gastrointestinal adverse events **(0.5% of all patients in SAS; 1.1.% of patient without gastroprotection medication).** These 16 patients with gastrointestinal adverse events represent 72.7% of all patients with gastrointestinal adverse events in this study and 13 patients represent 68.7% of all patients with gastrointestinal adverse reaction in the study.

Overall the treatment with Krka's naproxen sodium was well tolerated and **only 0.9% of patients (n=30) experienced adverse reactions related to Krka's naproxen sodium.**

Conclusion

At 2nd data capture physicians for approximately 44% assessed the response to Krka's naproxen sodium as very much improved since the initiation of treatment (n=1344; 43.6%), while for more than 46% patients they assessed their condition as much

improved (n=1424; 46.2%), for 8.7% patients there was reported minimal improvement (n=267) and for 1.3% stated no change from baseline (n=40). Only for 0.1% patients they assessed their response to Krka's naproxen sodium as minimally worse (n=3) and much worse (n=2). For one patient there was assessed the condition as very much worse.

At the end of observation more than **92.4% of patients were very satisfied or satisfied** with the treatment with Krka's naproxen sodium.

High levels of patient satisfaction and significant improvements in condition assessments by investigators further validate the positive impact of naproxen sodium on patient outcomes.

Krka's naproxen sodium 550 mg (Nalgesin® forte) remains a well-established, evidence-based option for patients requiring effective and well-tolerated pain management in LBP and OA, offering both effective pain reduction and significant improvements in functional capacity for daily activities. Additionally, it can serve as an effective monotherapy or as part of a comprehensive multimodal pain therapy, making it a versatile choice for individualized patient management.

LBP patients

Patients' demographic characteristics (age and sex) at the time of inclusion in the study

Out of 3081 patients on 1st data capture, 64.5% (n=1988) patients were diagnosed with low back pain. More than half of them were **female** (**56.8%**, n=1130), **43.2%** were **male** (n=858). Average age of patients was **51.2 ± 14.5 years**. For one patient there was no collected data about years.

Patients were divided into 5 groups according to their age.

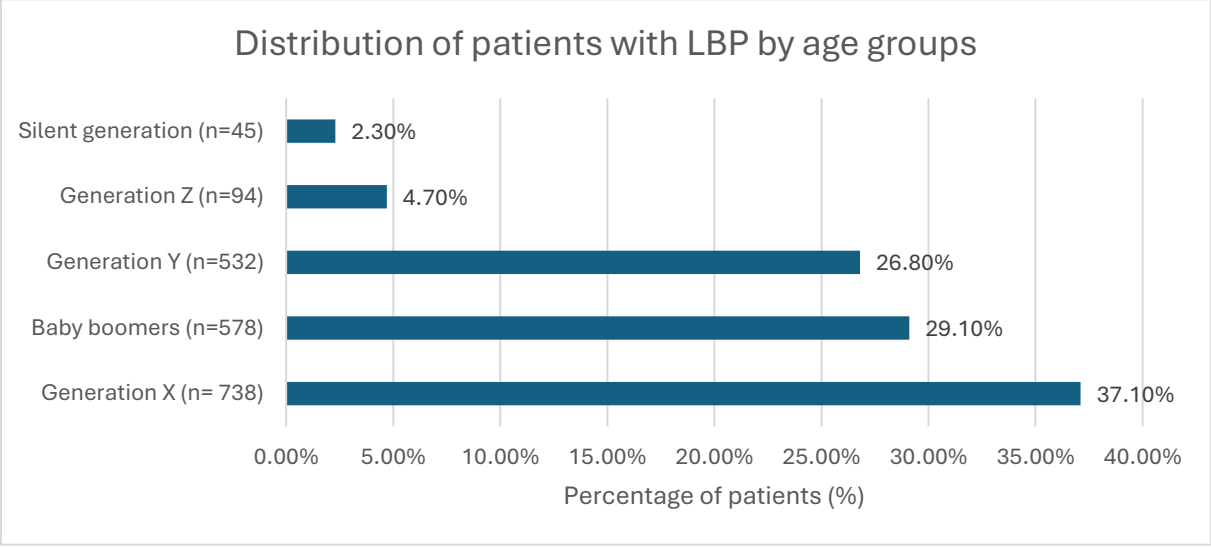

Figure 3: Distribution of patients with LBP by age groups.

Dosage regimen

At **1st data capture**, regardless to their specialty, investigators have most often prescribed a dose of Krka's naproxen sodium 550mg **twice a day** (n=1830; **92.1%**) to patients with LBP. Dosing regimen of once a day was prescribed to 6.7% (n=134) of patients with LBP and 1.2% of patients (n=24) were treated with 3 doses of Krka's naproxen sodium 550mg per day.

To all patients treated by **orthopaedist** (n=83; 100%), was prescribed dosing regimen of Krka's naproxen sodium 550mg twice a day. Investigators of **other specialty** have prescribed 2 doses per day to 97.2% of patients that they have treated (n=381), followed by 2.6% of patients (n=10) that received 1 dose per day. Only 1 patient was receiving 3 doses per day (0.3%). **Neurologists** prescribed 2 doses per day to 92.1% (n=233) of their patients, followed by dosing regimen of 3 doses per day (n=12; 4.7%). Only 8 of their patients (3.2%) were prescribed 1 dose per day. Most of all patients with LBP were treated by **general practitioners**, who most often prescribed a twice-daily dosing regimen (n=1054; 91.2%). Less than 8% of their patients were receiving 1 dose per day (n=91; 7.9%) and only 1.0% of their patients were taking 3 doses of Krka's naproxen sodium 550mg per day (n=11). 104 patients with LBP at 1st data were treated by **rheumatologists,** whose most often prescribed dosage regimen was 2 doses per day to 76.0% of their patients (n=79), followed by prescribed 1 dose per day to 24.0% of their patients (n=25). None of their patients was treated with 3 doses of Krka's naproxen sodium per day. Figure 4 shows distribution of patients with LBP by number of doses of Krka's naproxen sodium 550 mg at 1st data capture per investigator's specialty.

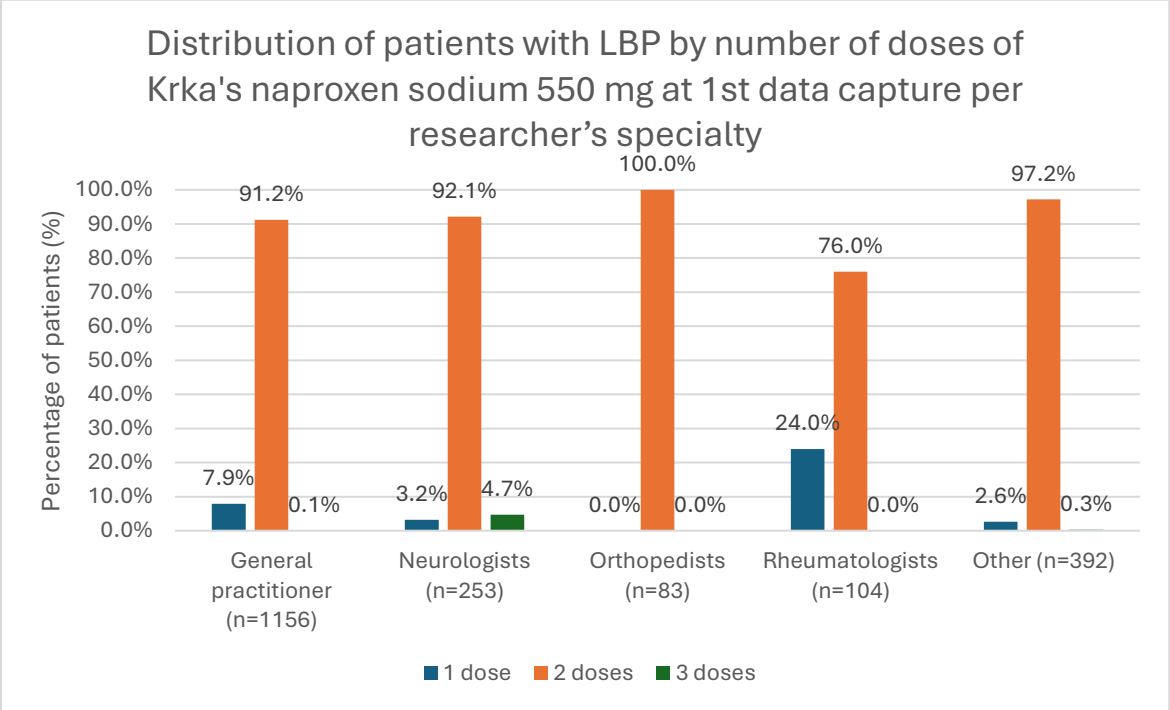

Figure 4: Distribution of patients with LBP by number of doses of Krka's naproxen sodium 550 mg at 1st data capture per investigator's specialty

Distribution of dosage regimen among all patients with LBP on **2nd data capture** (n=848) has changed by different specialty of investigators. 2-times-daily dosage regimen remained most often prescribed, where more than half of patients were receiving Krka's naproxen sodium 550mg **twice a day** (n=442; **52.1%**). Approximately 48% were taking 1 dose per day (n=404; 47.6%) and no patients has been prescribed 3 doses of Krka's naproxen sodium 550mg per day.

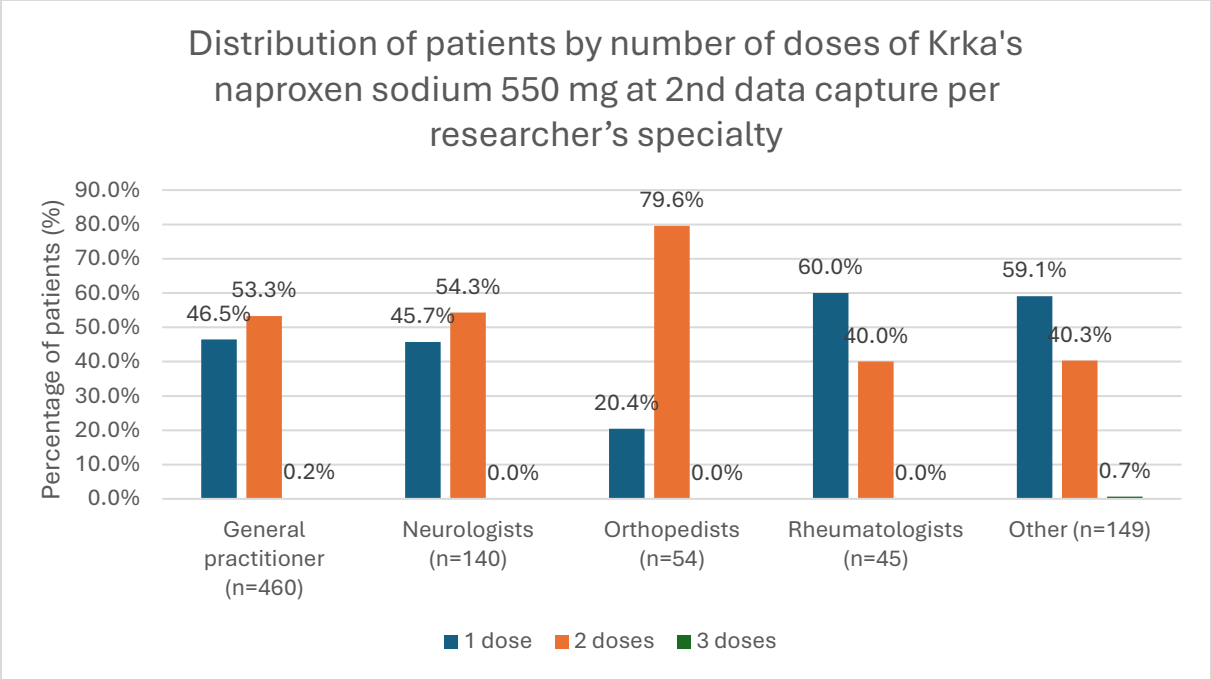

Figure 5: Distribution of patients by number of doses of Krka's naproxen sodium 550 mg at 2nd data capture per investigator's specialty.

Results

The data about impact of pain on all daily activities were collected for 1987 patients with LBP.

642 out of 732 **(87.7%) patients with LBP** with treatment duration at most 14 days reported improved abilities to perform overall activities of daily living.

After a 4-week treatment with Krka's naproxen sodium 550mg, **92.0%** (n=1828) **patients with LBP** reported **improved ability to perform overall daily activities**. 92.4% female patients (n=1044) and 91.4% male patients (n=784) reported improved ability to perform overall daily activities.

By improving the ability to perform daily activities, the positive effects of treatment with Krka's naproxen sodium 550mg were reflected in mobility, daily routines, socialization, and overall well-being. In total 1794 patients (**90.2%**) with LBP reported **improved mobility**, 1755 (**88.3%**) experienced better **daily routine**, **socialization** improved in

1606 patients (**80.8%**) and **general well-being/mood swings** were better in 1721 patients with LBP (**86.6%**).

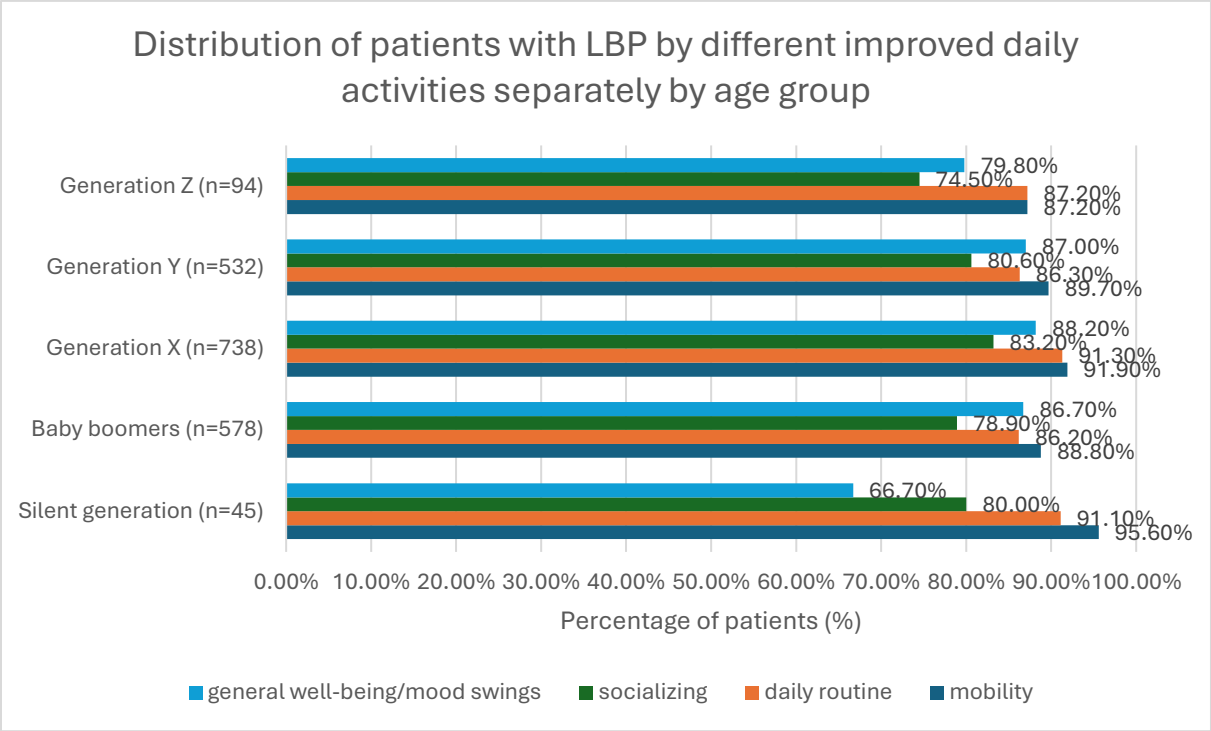

Figure 6: Distribution of patients with LBP by different improved daily activities separately by age group

Mean absolute and relative changes in scores measuring the impact of LBP on the ability to perform activities of daily living in total and in partial scores from the beginning to the end of an up to 4-week treatment with Krka's naproxen sodium are presented in Table . **The decreases in all scores were statistically significant** (p<0.001).

Table 5: Mean absolute and relative changes in scores measuring the impact of LBP on the ability to perform activities of daily living.

Pain impact scores	Nu. of patients with data	Mean values				95%-CI for mean absolute difference	p-value
		Scores at 1st and 2nd data capture		Abs. difference	Rel. difference		
Mobility	1988	14.27	8.1	-6.16	-41%	[-6.35,-5.97]	<0.001
Daily routine	1988	12.58	7.15	-5.44	-41%	[-5.62,-5.25]	<0.001
Socializing	1987	5.99	3.45	-2.54	-38%	[-2.64,-2.44]	<0.001
General well-being and mood swings	1987	8.68	5.05	-3.63	-39%	[-3.76,-3.5]	<0.001
OVERALL	1987	41.52	23.74	-17.78	-41%	[-18.33,-17.23]	<0.001

Pain intensity

Patients' mean of current pain intensity on NRS was for LBP patients at **1st data capture** (n=1988) **5.8 ± 1.7**, the mean value of average pain intensity in the last 24 hours **5.8 ± 1.7** and the mean value of worst pain intensity in the last 24 hours was **6.5 ± 1.8**.

At **2nd data capture** mean value of patients' current pain intensity on NRS was for LBP patients (n=1988) **2.0 ± 1.6**. Mean value of average pain intensity in the last 24 hours was **2.0 ± 1.5** and mean value of worst pain intensity in the last 24 hours was **2.5 ± 1.8**. For all three pain intensities the minimum recorded value was 0 and the maximum recorded value was 9 for current pain intensity and average pain intensity in the last 24 hours and 10 for worst pain intensity in the last 24 hours.

When comparing pain intensities between both data captures, **statistically significant decreases (p<0.001) were observed for all of them**.

Table 6 and Figure present changes in pain intensity for LBP patients with data for both data captures.

Table 6: Changes in pain intensity for LBP patients with data for both data captures.

Type of pain intensity on NRS scale	N	Mean values				95%-CI for mean absolute difference	p-value
		1st and 2nd data capture		Abs. difference	Rel. difference		
Current pain intensity	1988	5.79	1.97	-3.82	-65%	[-3.91,-3.74]	<0.001
Average PI in the last 24 hours	1988	5.76	2.02	-3.74	-64%	[-3.83,-3.65]	<0.001
Worst PI in the last 24 hours	1988	6.5	2.46	-4.04	-61%	[-4.13,-3.95]	<0.001

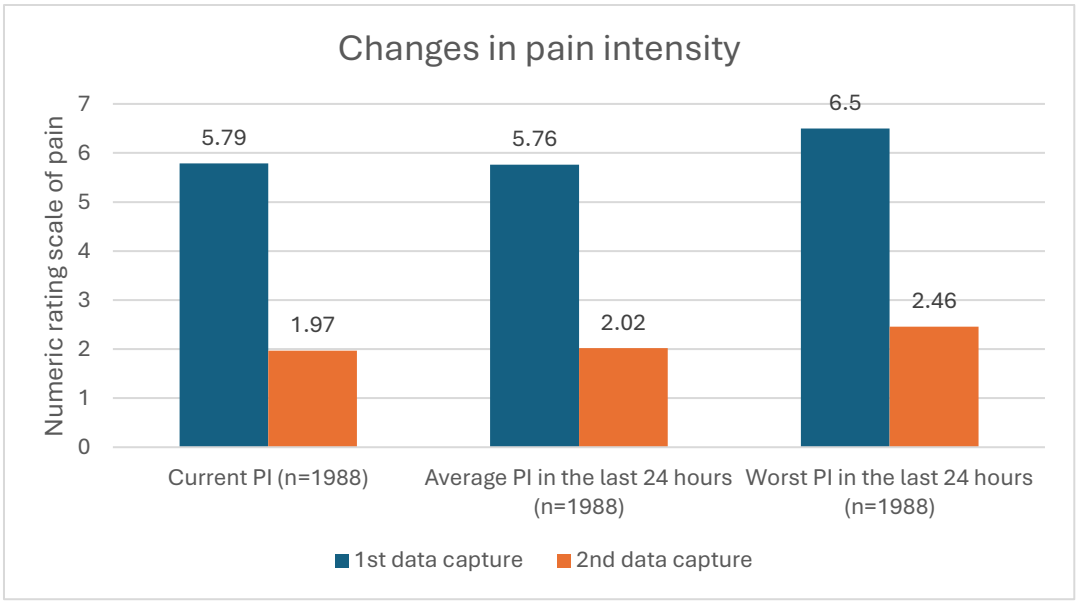

Figure 7: Changes in different pain subscales on 1st and 2nd data capture for patients with LBP.

OA patients

OA Patients' demographic characteristics (age and sex) at the time of inclusion in the study

Out of 3081 patients on 1st data capture, 35.5% (n=1093) patients were diagnosed with painful osteoarthritis. Of those 35.5% of patients with painful osteoarthritis, 8.0% (n=246; 22.5% of patients with OA) of all patients had hand osteoarthritis. 4.4% (n=136; 12.4% of patients with OA) had hip osteoarthritis, 17.9% (n=552; 50.5% of patients with OA) had knee osteoarthritis and others (5.2%; n=159; 14.5% of patients with OA) had other osteoarthritis.

Almost 70% of them were **female** (**69.4%,** n=758) and **30.6%** were **male** (n=335). Average age of patients was **58.7 ± 13.3 years**.

Patients were divided into **5 groups according to their age**. 4.6% (n=50) of patients were born between 1928 and 1945 and were part of silent generation. 48.8% (n=533) were baby boomers (born between 1946 and 1964), 33.8% (n=369) of patients were born in the years 1965 and 1980 (generation X), 10.2% (n=112) were generation Y (year of birth between 1981 and 1996) and 2.7% (n=29) of patients belong to generation Z (born between 1997 and 2006). Figure presents distribution of patients with OA by age groups.

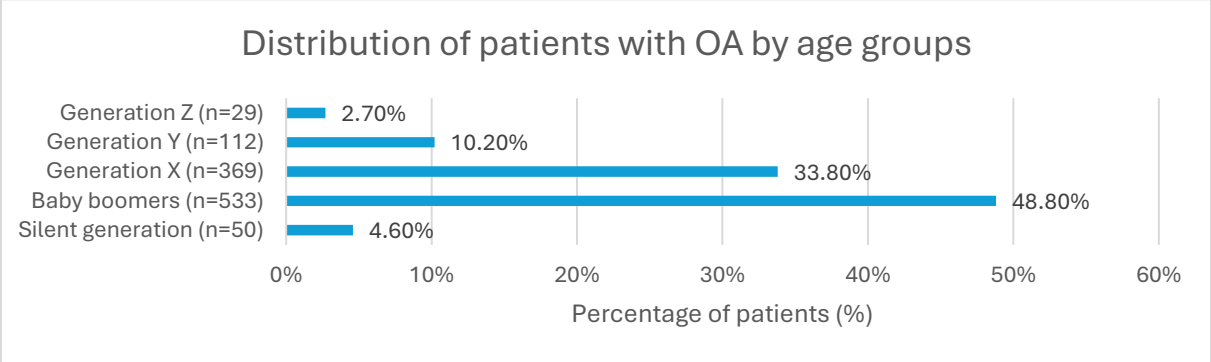

Figure 8: Distribution of patients with OA by age groups.

Dosage regimen

At **1st data capture**, regardless to their specialty, investigators have most often prescribed a dose of Krka's naproxen sodium 550mg twice a day (n=987; 90.3%) to patients with OA. Dosing regimen of once a day was prescribed to 9.4% (n=103) of patients with LBP and 0.3% of patients (n=3) were treated with 3 doses of Krka's naproxen sodium 550mg per day.

To all patients treated by **orthopaedists** (n=83; 100%) and **neurologists** (n=45; 100%) was prescribed dosing regimen of Krka's naproxen sodium 550mg twice-a-day.

Investigators of **other specialty** have prescribed 2 doses per day to 97.3% of patients that they have treated (n=182), followed by 2.1% of patients that received 1 dose per day. Only 1 patient was receiving 3 doses per day (0.5%). Little less than half of all patients with OA were treated by **general practitioners**, who most often prescribed a twice-daily dosing regimen (n=417; 91.0%). Less than 10% of their patients were receiving 1 dose per day (n=39; 8.5%) and only 0.4% of their patients were taking 3 doses of Krka's naproxen sodium 550mg per day (n=2). 320 patients with OA at 1st data were treated by **rheumatologists,** whose most often prescribed dosage regimen was 2 doses per day to 81.3% of their patients (n=260), followed by prescribed 1 dose per day to 18.8% of their patients (n=60). None of their patients was treated with 3 doses of Krka's naproxen sodium per day. Figure 9 shows distribution of patients with OA by number of doses of Krka's naproxen sodium 550 mg at 1st data capture per investigator's specialty.

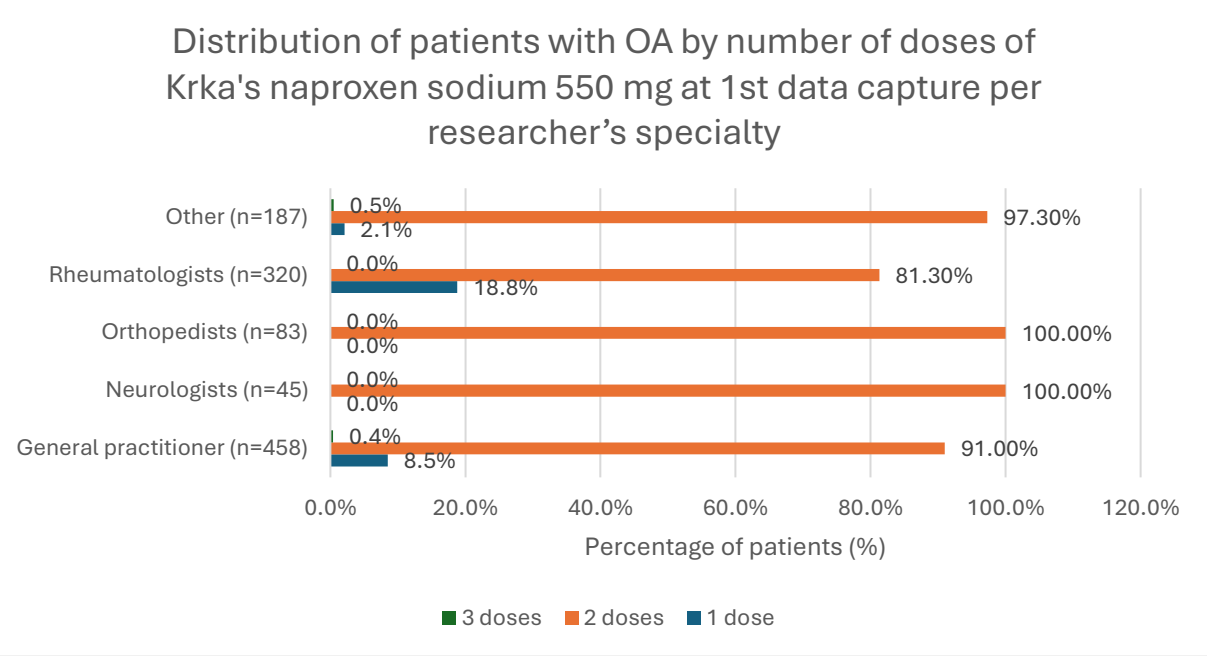

Figure 9: Distribution of patients with OA by number of doses of Krka's naproxen sodium 550 mg at 1st data capture per investigator's specialty.

Distribution of dosage regimen among all patients with OA on **2nd data capture** (n=472) has changed by different specialty of investigators. 2-times-daily dosage regimen remained most often prescribed, where more than half of patients were receiving Krka's naproxen sodium 550mg twice a day (n=238; 50.4%). Approximately 49% were taking 1 dose per day (n=233; 49.4%) and 1 patient has been prescribed 3 doses of Krka's naproxen sodium 550mg per day (0.2%). **Orthopedists** were the only ones among all investigators that have prescribed dosage regimen of thrice-a-day (n=1; 1.7%). Majority of their patients remained on 2 doses of Krka's naproxen sodium per day (n=50; 84.7%), followed by 1 prescribed dose per day for 13.6% of their patients (n=8). Twice-daily

dosing regimen also remained most often prescribed regimen by **neurologists** (n=17; 68.0%). They have prescribed dosage regimen of once-per-day to 32.0% (n=8) of their patients. At 2nd data capture **general practitioners** changed their prescription for the number of doses of Krka's naproxen sodium 550 mg from 1st data capture. Most often prescribed dosage regimen was 1 dose per day for 50.7% for their patients (n=108) and 49.3% (n=105) were receiving 2 doses per day. Similar distribution of dosage regimen was with patients treated investigators from **another speciality**. 53.4% of their patients (n=47) also received one dose per day, 46.6% were taking 2 doses per day (n=41). **Rheumatologists** treated 71.3% of their patients (n=62) with 1 dose and 28.7% (n=25) with 2 doses of Krka's naproxen sodium per day. Figure shows distribution of patients with OA by number of doses of Krka's naproxen sodium 550 mg at 2nd data capture per investigator's specialty.

Distribution of dosage regimen among all patients with OA on **2nd data capture** (n=472) has changed by different specialty of investigators. 2-times-daily dosage regimen remained most often prescribed, where more than half of patients were receiving Krka's naproxen sodium 550mg twice a day (n=238; 50.4%). Approximately 49% were taking 1 dose per day (n=233; 49.4%) and 1 patient has been prescribed 3 doses of Krka's naproxen sodium 550mg per day (0.2%).

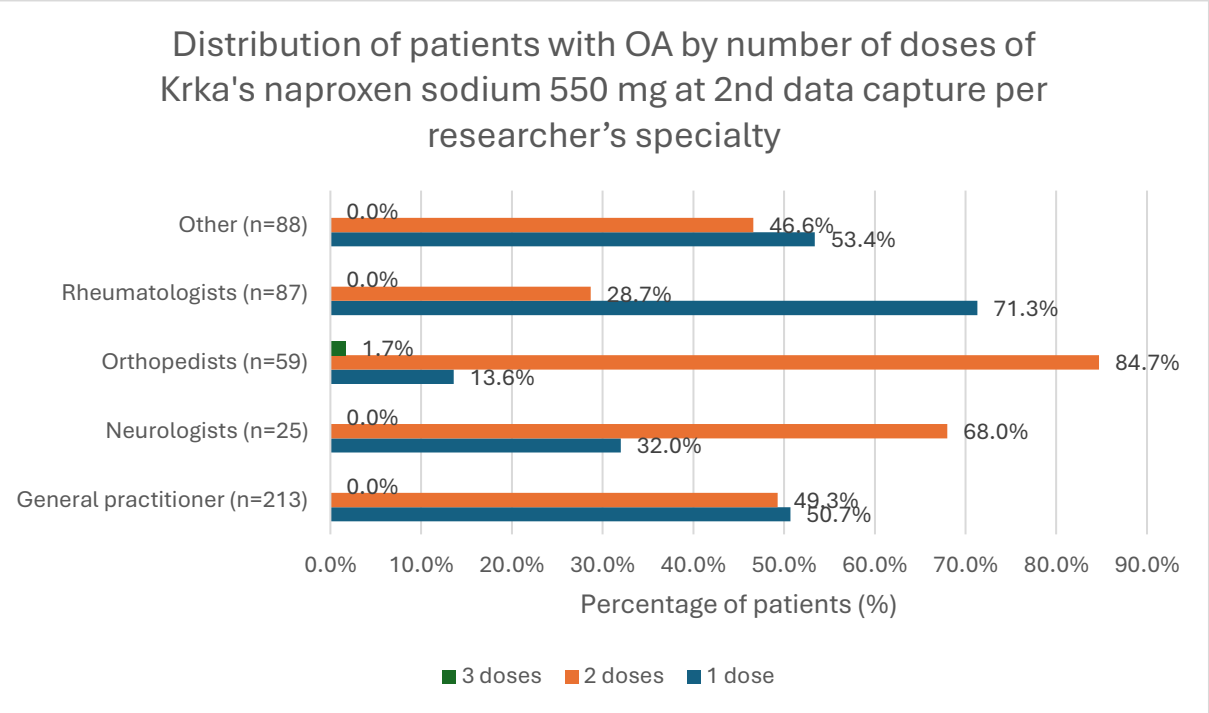

Figure 10: Distribution of patients with OA by number of doses of Krka's naproxen sodium 550 mg at 2nd data capture per investigator's specialty.

Results

324 out of 374 **(86.6%) patients with OA** with treatment duration at most 14 days reported improved abilities to perform overall activities of daily living.

The data about impact of pain on all daily activities were collected for 1093 patients with OA. After a 4-week treatment with Krka's naproxen sodium 550mg, **90.9% (n=994) patients with OA** reported **improved ability to perform overall daily activities**. 90.5% female patients (n=758) and 91.9% male patients (n=335) reported improved ability to perform overall daily activities.

Table 7: Patients with OA based on different subgroups, who reported improved overall daily activities.

	LBP Patients with data	Nu. of LBP patients with improvement	% of LBP patients with improvement	95%-CI
LBP patients based on pain intensity				
24h API equal to 3	129	119	92.2%	[86.2%,96.2%]
24h API 4 to 6	601	550	91.5%	[89.0%,93.6%]
24h API 7 to 10	363	325	89.5%	[85.9%,92.5%]
LBP patients based on age groups				
Silent generation	50	45	90.0%	[78.2%,96.7%]
Baby boomers	533	478	89.7%	[86.8%,92.1%]
Generation X	369	337	91.3%	[88.0%,94.0%]
Generation Y	112	107	95.5%	[89.9%,98.5%]
Generation Z	29	27	93.1%	[77.2%,99.2%]

By improving the ability to perform daily activities, the positive effects of treatment with Krka's naproxen sodium 550mg were reflected in mobility, daily routines, socialization, and overall well-being. In total 973 patients (**89.0%**) with OA reported **improved mobility**, 953 (**87.2%**) experienced better **daily routine**, **socialization** improved in 796 patients (**72.8%**) and **general well-being/mood swings** were better in 920 patients with OA (**84.2%**).

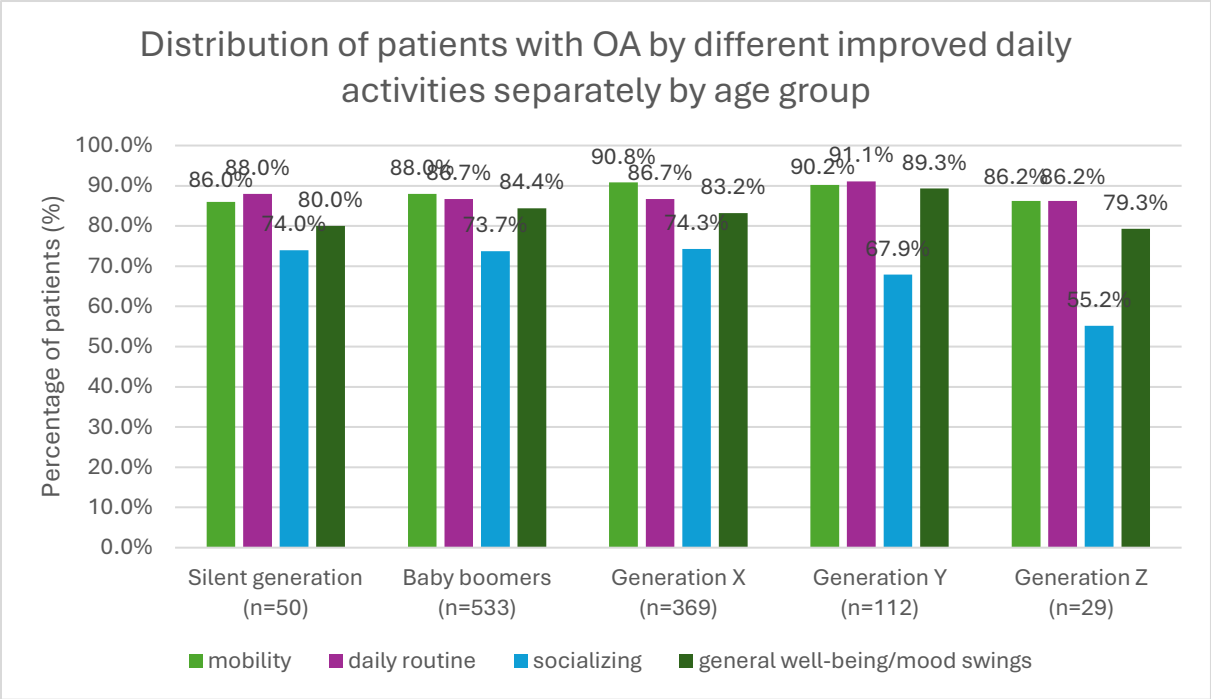

Figure 11: Distribution of patients with OA by different improved daily activities separately by age group.

Mean absolute and relative changes in scores measuring the impact of OA on the ability to perform activities of daily living in total and in partial scores from the beginning to the end of an up to 4-week treatment with Krka's naproxen sodium are presented in Figure 11. **The decreases in all scores were statistically significant** (p<0.001).

Pain intensity

Patients' mean of current pain intensity on NRS was for OA patients at **1st data capture** (n=1093) **5.6 ± 1.8**, the mean value of average pain intensity in the last 24 hours **5.6 ± 1.8** and the mean value of worst pain intensity in the last 24 hours was **6.3 ± 1.9**.

At **2nd data capture** mean value of patients' current pain intensity on NRS was for OA patients (n=1093) **2.1 ± 1.5**. Mean value of average pain intensity in the last 24 hours was **2.2 ± 1.5** and mean value of worst pain intensity in the last 24 hours was **2.6 ± 1.7**. For all three pain intensities the minimum recorded value was 0 and the maximum 9.

When comparing pain intensities between both data captures, **statistically significant decreases (p<0.001) were observed for all of them**.

Table 8 and Figure 12 present changes in pain intensity for OA patients with data for both data captures.

Table 8: Changes in pain intensity for OA patients with data for both data captures.

Type of pain intensity on NRS scale	N	Mean values				95%-CI for mean absolute difference	p-value
		1st and 2nd data capture		Abs. difference	Rel. difference		
Current pain intensity	1093	5.6	2.15	-3.45	-60%	[-3.57,-3.34]	<0.001
Average PI in the last 24 hours	1093	5.62	2.18	-3.44	-60%	[-3.56,-3.32]	<0.001
Worst PI in the last 24 hours	1093	6.26	2.61	-3.66	-57%	[-3.78,-3.53]	<0.001

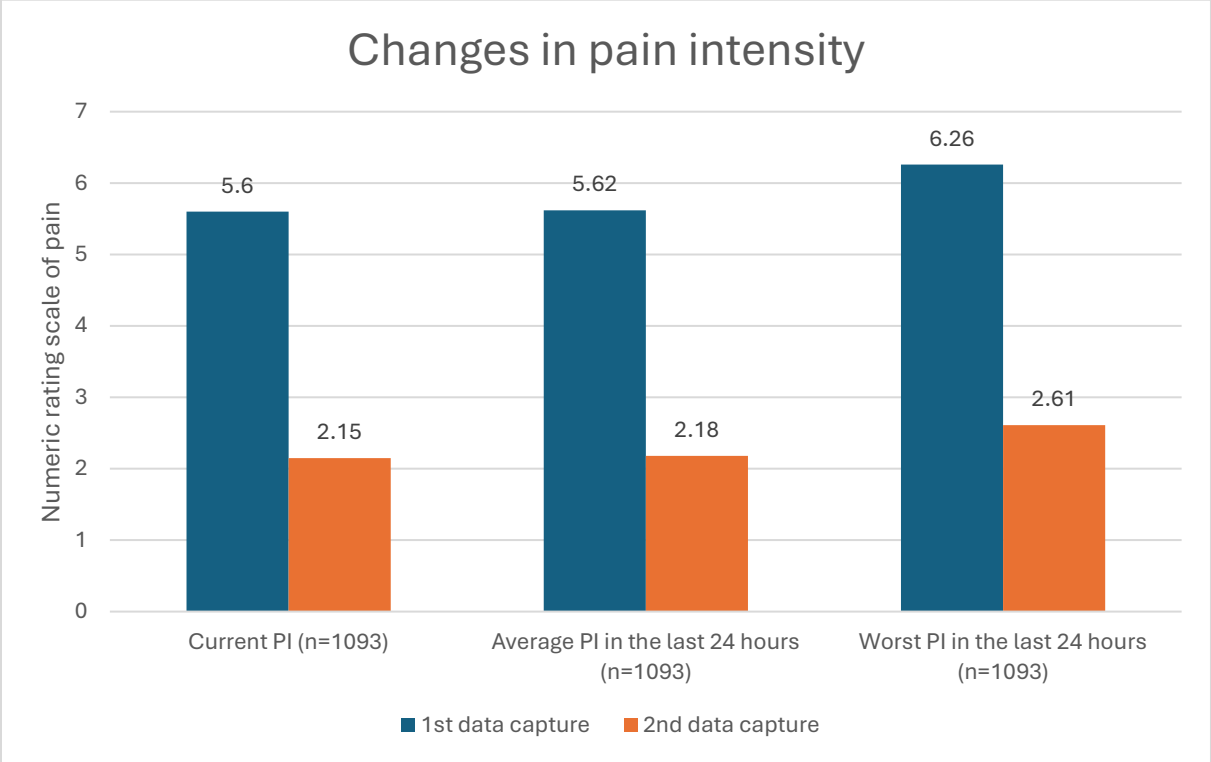

Figure 12: Changes in different pain subscales on 1st and 2nd data capture for patients with OA.

Conclusion

The results of this study underscore the significant benefits of Krka's naproxen sodium 550 mg (Nalgesin® forte) in managing low back pain (LBP) and osteoarthritis (OA). The study's comprehensive approach, involving a diverse patient population and various clinical settings, provides robust evidence for the efficacy and safety of this treatment.

At the end of observation more than **92.4% of patients were very satisfied or satisfied** with the treatment with Krka's naproxen sodium.

Key insights from the study include:

Generational Differences: The prevalence of LBP among younger generations (Generation Y and X) contrasts with the higher incidence of OA in older generations (Baby Boomers and Silent Generation). This demographic insight underscores the need for age-specific approaches in managing these conditions.

Functional Improvement: Over 90% of patients reported improved ability to perform daily activities after up to 4 weeks of treatment, with minimal differences between genders and baseline pain intensities. Generation X showed slightly higher improvement, likely due to their higher baseline activity levels compared to older generations, while placing less emphasis on daily activities than younger generations. Socializing and mood swings/general well-being showed the lowest improvement across all groups due to the fact that these two factors are more challenging to address in the short term.

Pain Reduction: Statistically significant reductions in pain intensities were observed, with current pain intensity decreasing by 63%, average pain intensity in the last 24 hours by 62%, and worst pain in the last 24 hours by 60%. These results affirm the effectiveness of naproxen sodium in managing pain.

Prescription Practices: Initially, treatment regimens were predominantly twice daily (with once-daily use being less common). On second data capture once-daily treatment became nearly as frequent, likely due to reduced pain and improved function diminishing the need for more frequent interventions.

Combination Therapy: Despite the potent effects of naproxen sodium, approximately 30% of patients required additional analgesic treatments, highlighting the importance of individualized treatment approaches.

Patient Satisfaction: High levels of patient satisfaction (92.4%) and significant improvements in condition assessments by investigators further validate the positive impact of naproxen sodium on patient outcomes.

Safety Profile: The treatment was well tolerated, with a low incidence of adverse reactions. Gastroprotective measures were effective in minimizing gastrointestinal adverse reactions.

In conclusion, Krka's naproxen sodium 550 mg (Nalgesin® forte) remains a well-established, evidence-based option for patients requiring effective and well-tolerated pain management in LBP and OA, offering both effective pain reduction and significant improvements in functional capacity for daily activities. Additionally, it can serve as an effective monotherapy or as part of a comprehensive multimodal pain therapy, making it a versatile choice for individualized patient management.