



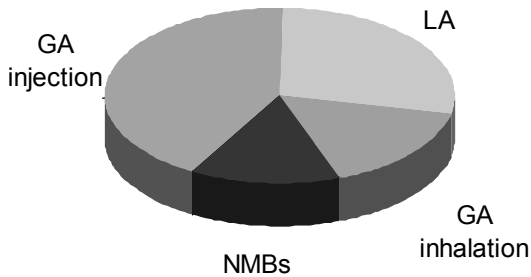
AstraZeneca Pain Control
Carl-Johan Dalsgaard
Vice President & Head of Pain TA

Vision

- Maintain and develop leadership in anaesthesia
- Novel therapies in analgesia meeting high unmet medical needs
- Focus on nociceptive and neuropathic pain

Leading company in pain control worldwide

An anaesthesia portfolio that meets market trends



Total value \$2.8bn

- AstraZeneca has 40% market share
- The trends are
 - increased day case surgery
 - early mobilisation
 - increased use of i.v. and regional anaesthetics

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Diprivan® - the leading i.v. anaesthetic

Defend the existing business with Diprivan® EDTA

product is registered in 11 countries, equivalent to 66% of all Diprivan® sales

patents approved in 5 countries and pending in 15

appeal against Gensia-Sicor approval

Increase market share

optimise product presentation for each market segment

ICU sedation

maximise synergies with local anaesthetic

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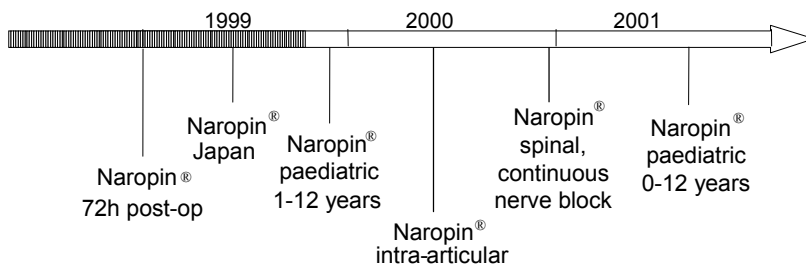
Diprivan® EDTA

Slide unpublished



Naropin® - first single enantiomer in local anaesthesia

Approved in 50 countries, launched in 38
Product development through sNDAs



Sales growth +65% (9 mths 99 vs 9 mths 98)



Naropin® opportunities in pain control

Satisfactory pain control after major abdominal surgery

70% with Naropin® alone
90% with Naropin® + fentanyl



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Statistically significant difference in ability to walk from day one
All Naropin® patients were able to walk day 2



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Improved outcome vs inhalation anaesthesia and systemic opioids
after hip replacement
Shorter post-operative intensive care
2 days vs 4 days to regain GI function

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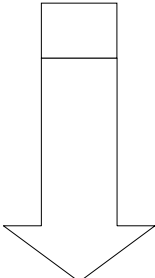
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Naropin® shows less cardiotoxicity than levobupivacaine

Resuscitation after cardiovascular collapse in the dog

	Plasma conc at cardiovascular collapse (µg/ml)	Ventricular fibrillation during resuscitation	Death	
	Naropin®	38	0/10	1/10
	levobupivacaine	24	2/10	3/10
	bupivacaine	22	4/10	5/10

Increased toxicity

L. Groban et al. ASA, 1999, A-886

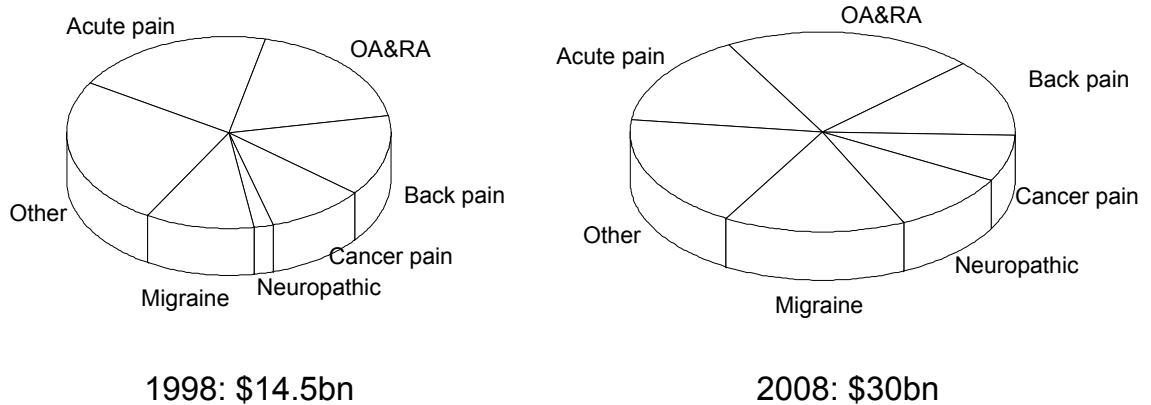
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Maintain and develop leadership in anaesthesia

- Worldwide roll out of Diprivan® – EDTA
- Aggressive defence of patents and SPC's
- Expand Naropin® usage into post-operative pain management
- Active lifecycle management of Naropin® with new indications
- Dedicated sales resource and an attractive licensing partner

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Opportunities in analgesia



Innovative approaches to the 3 key medical needs of analgesia

- Strong analgesic without opioid side effects
- Effective treatment for neuropathic pain
- Effective NSAID without GI side effects

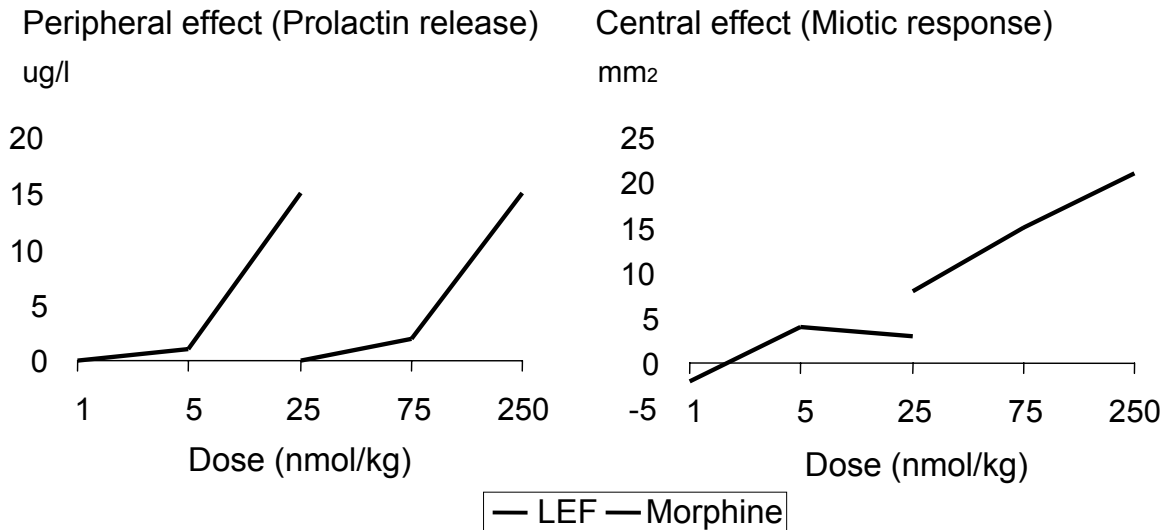
Innovative approaches to the 3 key medical needs of analgesia

- Strong analgesic without opioid side effects LEF
- Effective treatment for neuropathic pain EP1
- Effective NSAID without GI side effects NO-NSAID

LEF - strong analgesic without opioid side effects

- Peripheral μ -opioid analgesia without CNS mediated side effects e.g. respiratory depression, dependence, nausea and vomiting
- μ -opioid receptors are upregulated in inflamed tissues
- Locally administered morphine gives analgesia at low (nonsystemic) concentrations
- Does not pass blood brain barrier in man
- Concept studies are under way, NDA (injectable) 2002
- Substance patent protection 2017

LEF does not pass blood brain barrier in man



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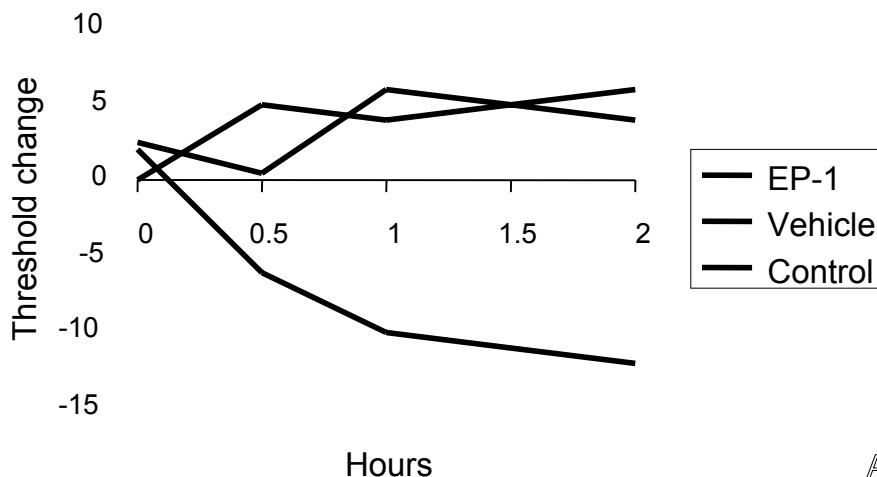
EP-1 antagonist for treatment of neuropathic pain

Blocks central prostaglandin E1 receptors
Shows analgesia in neuropathic pain models in animals
Blocks central sensitisation in human volunteer model
Concept studies ongoing, NDA 2003
Substance patent protection 2016

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EP-1 antagonist blocks central sensitisation

Pain thresholds in human volunteer model



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NO-NSAID - a unique approach to nociceptive pain

Both COX1 and COX2 inhibition is required for full pain relief
in inflammatory conditions

NO (nitric oxide) counteracts NSAID's harmful effects on
gastric mucosa

Animal data show superior efficacy to COX2 inhibitors

Animal data show remarkably good gastric profile

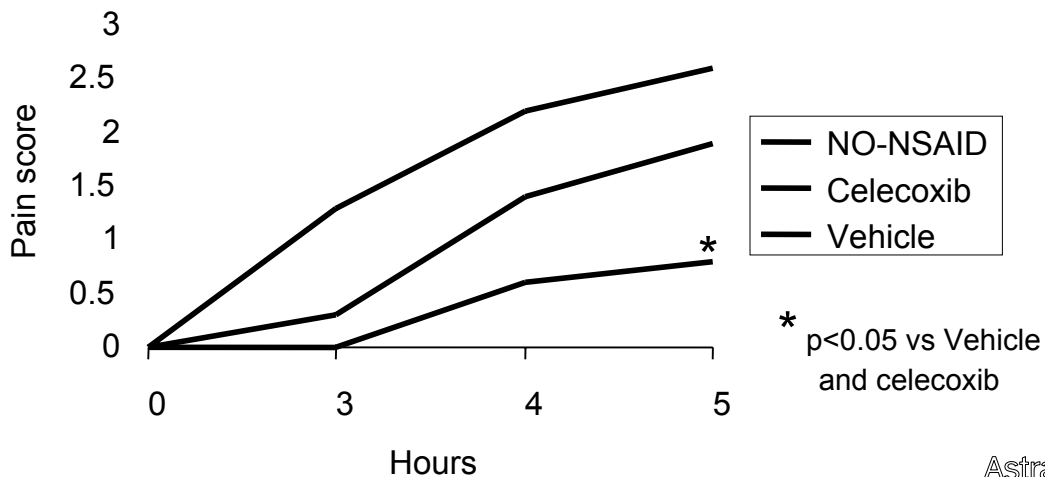
Entering clinical trials H1 2000, NDA 2003

Substance patent protection 2015-2017

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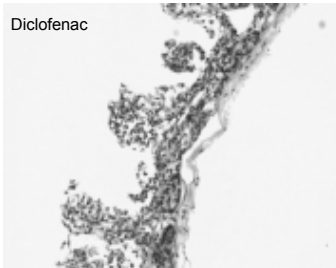
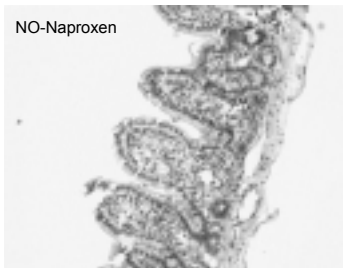
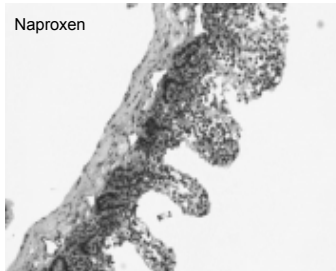
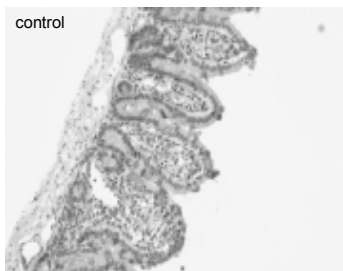
NO-NSAID is more effective than COX2 in the rat

Carrageenan arthritis in rat - pain behaviour



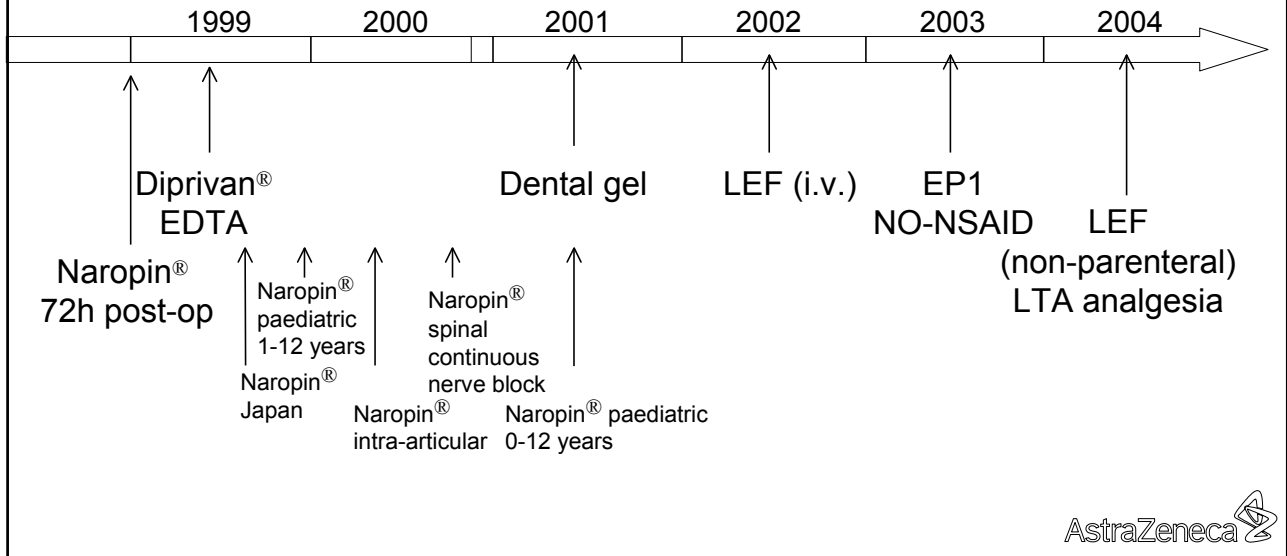
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NO-NSAID show good GI tolerability in animals



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Summary of pain control portfolio (NDAs)



- Maintain and develop leadership in anaesthesia
- Introduce novel and complementary approaches to analgesia meeting the 3 highest unmet medical needs

Leading company in pain control worldwide

